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GENERAL PRACTICE CLINICS

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SYMPOSIUM ON DEVELOPMENTAL DISORDERS IN CHILDREN
Their Mechanism and Management
Guest Editor—I. Newton Kugelmass, M.D., Ph.D., Sc.D.

Introduction — I. Newton Kugelmass
Congenital Anomalies in the Newborn Infant: Their Early Recognition in Relation to Prognosis — W. S. Craig
Experimental Production of Congenital Malformations — Josef Warkany
Psychochemotherapy of Mental Deficiency in Children — I. Newton Kugelmass
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FELIX MARTI-IBAÑEZ, M.D., Editor

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SYMPOSIUM ON DEVELOPMENTAL DISORDERS IN CHILDREN

THEIR MECHANISM AND MANAGEMENT

Introduction

I. Newton Kugelmass, M.D., Ph.D., Sc.D.

CONSULTANT TO THE DEPARTMENT OF HEALTH AND HOSPITALS

NEW YORK, N. Y.

In Nature there's no blemish but the mind;
None can be called deformed but the unkind.
[Shakespeare, Twelfth Night]

Congenital malformations are common afflictions that treatment may alleviate or cure but that more complete understanding can abolish. The infinite varieties of congenital anomalies in the animal body arise from its inexplicable pattern of development. Animals grow in a most complicated manner in comparison with plants, which attain final form by adding cell to cell. Most animal structures are formed and then vanish without apparent function. Some organs are built up in one place, and then migrate to a different site. Even the construction of the most essential tissues depends on the meeting and fusion of processes emanating from widely separated points. It is little wonder that so many anomalies appear during this difficult period of differentiation of structure and function of the fetal organism.

The first trimester of pregnancy is the period of greatest susceptibility to serious injury in structural development, since the later periods are devoted to mere accretion. A family possessing one child with a malformation shows 20 times the frequency of anomalies than a family with no such developmental history. Failure of formation of a part of the body is irreparable, although surgery may provide some efficient substitute. Extra formations are readily amenable to surgical modification. Failure of fusion, migration, or atrophy creates special difficulties not always amenable to repair. Deformities of mechanical origin, such as excessive hydraulic packing of the child or the undue resistance to expansion of the fetal limbs, remain a neglected field of study. Anomalies of chemical origin are being reproduced experimentally to delineate their mechanism and management.

TABLE I

Developmental Disorders—Hereditary and Acquired

Genetic disorders	Genetic-environmental disorders	Environmental disorders
Abiotrophies	Biochemical anomalies (some)	Functional anomalies (some)
Congenital defects (some)	Blood disorders (some)	Infections (some)
Endocrine disorders (some)	Congenital defects (some)	Neoplasms (some)
Functional anomalies (some)	Endocrine disorders (some)	Traumatic disorders
Neoplasms (some)	Infections (some)	
Phacomatoses		

Genetically determined diseases are not finished entities at birth. Many hereditary affections are not congenital but begin after birth and are relentlessly progressive, i.e., retinitis pigmentosa, myotonia atrophica, or Huntington's chorea. Furthermore, the congenital anomaly present at birth does not arise as a finished entity but is merely the end stage of an evolutionary process that has run to its conclusion in antenatal life. Even then, some congenital malformations show progressive postnatal changes, such as increasing crippling in osteogenesis imperfecta. The study of these disorders calls for more than the recognition of the casual relationship between the pathogenic gene and the end stage; the entire dynamic process, prenatal or postnatal, must be unraveled.

Environmental causes of congenital anomalies are evident in intrauterine infections, irradiations, toxoplasmosis, prematurity, and chemical disorders. Relatively few affections are entirely environmental in origin. Indeed, inheritance is now characterizable in terms of transmission of control of relative rates of biochemical reactions within complex and interlocked metabolic patterns, which determine the caliber of resistance to many pathologic processes including infections, neoplasms, deficiency diseases, and metabolic disorders. But children show a marked inherent drive to develop despite deterring genetic or environmental forces. (See table I.)

A child's developmental potentialities can be enhanced by proper medical supervision. It involves correction of congenital deficiencies or defects, maintenance of superior nutrition, provision of personalized psychologic care, integration of personality factors, in addition to the routine prophylactic and therapeutic procedures to combat disease. Pediatric supervision by periodic examinations thus entails an assessment of *developmental health* in terms of rates of maturation of the mental, physical, emotional, and social development as well as of *physical health* in terms of current constitutional status. The masterly series of contributions in this issue of the INTERNATIONAL RECORD OF MEDICINE AND GENERAL PRACTICE CLINICS is therefore dedicated to the inalienable right of every child to the fullest development of all his potentialities and, therefore, to the inherent right to demand of mankind whatever he needs to supplement his own efforts.

Congenital Anomalies in the Newborn Infant

Their Early Recognition in Relation to Prognosis

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"Will he be all right?" This is the inevitable question asked by the mother who has just been told that her newborn baby has a congenital anomaly. The mother is entitled to an honest answer provided always that the reply takes into account her emotional state and the physical strain through which she has passed. When congenital anomalies are present, it is often difficult to give a prognosis, since the parents will expect it to take into account long-term as well as immediate possibilities.

GENERAL CONSIDERATIONS

Thus the distress occasioned by a harelip can be dispelled by confident assurance concerning the outcome of operation. When the anomaly consists of a cleft palate, account must be taken of the feeding problems during the period preceding operation. Nevi can be a source of anxiety. Whatever the nature of the nevus, the parents can be assured that no threat to life is involved, but a firm opinion concerning the likelihood of some form of treatment being ultimately necessary may have to be delayed for a number of months. The reasons for postponing a final opinion should always be explained, if only to avoid giving a disturbing impression of concealment. Port-wine nevi rarely disappear; spider nevi frequently disappear; and strawberry nevi and cavernous angiomas usually disappear, though sometimes they increase in size; their partial disappearance may be accompanied by scarring or ulceration.

Congenital absence of the radius presents special problems. Straightening of the deformity for esthetic reasons, which naturally appeals to the parents, does not improve function and actually involves the risk of functional consequences comparing unfavorably with results in children not submitted to operation. A different situation arises when the baby has a talipes deformity. Inevitably the father and mother are perturbed but they cannot always be expected to appreciate the necessity for immediate treatment. In these circumstances it is necessary to convince the parents, without alarming them, of the need to promote optimum function in the future by agreeing to orthopedic correction without delay. Success of initial treatment is no guarantee that there will be no recurrence. Continuing orthopedic supervision in infancy and childhood is essential. A proportion of cases require operative intervention; surgical fixation after puberty is sometimes necessary.

In contrast is the newborn baby with clinical evidence of alimentary obstruction. The gravity of the situation is usually fully appreciated by the parents, who will accept without demur the decision to refer immediately to surgery. Despite the remarkable results now achieved by surgeons experienced in neonatal work and

assisted by advances in anesthesia, the seriousness of operative intervention in the early days of life should not be underestimated. Finally there are a few anomalies that are usually, although not invariably, incompatible with survival. These include meningomyelocele and congenital osteogenesis imperfecta.

ESSENTIALS IN PROGNOSIS

Prognosis is often no more than tentative; to be reasonably accurate it must take into account the infant's general condition. In particular, prematurity, more especially if the gestation period has been very short, adds to the seriousness of any anomaly interfering with normal respiratory, alimentary, or metabolic function. This also applies to immaturely developed infants of a multiple pregnancy. Detection of an anomaly calls for examination for malformations elsewhere, and allowance must be made for the implications of any that may be discovered. Thus in a baby with a cleft palate, the detection of a congenital heart anomaly is of greater significance than the presence of syndactylism. Infection, no matter where it is found, necessarily demands caution in prognosis. This is especially the case when the anomaly is the site of infection, as for example when urinary infection complicates a rectourethral or rectovesical fistula.

Prompt recognition is essential to sound prognosis except in the case of anomalies not involving a threat to life or risk of delayed physical handicap. Delivery of an infant should be followed after a short interval by clinical examination to exclude such anomalies as talipes, imperforate anus, and cleft palate. Other anomalies may present in other ways at varying periods of hours or days after birth—the return of fluids by mouth; the retention of meconium or feces; pallor or cyanosis, intermittent or persistent; respiratory embarrassment, to cite a few random examples. Early detection in these circumstances depends on constant alert awareness on the part of the clinical observer, whether doctor or midwife.

When a diagnosis has been made, prognosis must in many instances make allowance for the skill of the nursing services that will be available to the child. The feeding of very young infants with such conditions as severe cleft palate or marked micrognathia constitutes one of the most testing challenges to nursing skill. The fate of many babies with severe congenital heart disease often hangs precariously in the balance for a number of weeks. Many die. Those who survive infancy owe their lives to skilled nursing. Prognosis in conditions that require a thoracic or abdominal operation and that have been promptly diagnosed largely depends on the experience and skill of those undertaking surgical and nursing care. In making arrangements for transport of infants born at home, special attention must be paid to the need to avoid delay and to minimize risks of shock in order that hospital treatment may have the best chance of success.

PARTICULAR PROBLEMS

Anomalies of the heart are especially perplexing in the newborn child. Murmurs are frequently detected in the absence of a congenital heart anomaly, and they may not be heard for a number of days or even weeks after birth when a cardiac anomaly

does exist. Signs suggestive of a cardiac anomaly are frequently detected in infants without any evidence of embarrassment or impaired development. In these infants, a long-term prognosis must await repeated clinical examination over a period of months or years together with special investigations in selected cases.

Death frequently occurs within a few hours or days in cases in which persistent "central" cyanosis and severe anoxia of cardiac origin appear shortly after birth. Among infants with a congenital heart anomaly who survive the first week of life, the immediate prognosis is worse in those in whom cyanosis (of whatever degree) is constantly present. In other babies, cyanosis and distress are intermittent; there is reluctance to feed, and weight gain is stationary or slow. The majority of these infants die within one or two months of birth. In a way that cannot be predicted, a few, after existing precariously for some six weeks, suddenly improve and continue to do so. Enlargement of the heart or liver is prognostically grave, except in those instances where enlargement is secondary to paroxysmal tachycardia that can be rapidly controlled by digitalization. The difficulties of detailed diagnosis and of surgical technique have limited operative procedures in the early weeks and months of life.

Clinical signs suggestive of a cardiac anomaly are present in approximately 50 per cent of newborn mongol babies. Death within a few days is probable in infants with extreme inertia and pronounced cyanosis. Infants who survive the neonatal period are those in whom generalized hypotonia is least marked. Antibiotic therapy has greatly reduced the death rate due to infections at all ages among mongol children with cardiac anomalies. As a result, prognosis is concerned with innumerable domestic and social problems individual to each child.

Among intrathoracic conditions, congenital pulmonary cysts are best dealt with by early excision. Acute symptoms due to diaphragmatic hernia are an indication for immediate emergency operation. When symptoms are not so severe or constant, surgery involves less risk and can be postponed for a limited period. Operation is, however, essential to obviate the risk of intestinal obstruction. The great majority of umbilical hernias disappear spontaneously without treatment of any kind in the course of two years and rarely give rise to complications. Opinions differ concerning inguinal hernias. Some authorities consider strangulation to be not uncommon and they advocate early operation; others prefer to postpone surgical intervention until after the age of 18 months in cases in which spontaneous reduction has not taken place.

Deformities involving the spinal column are not uncommon. In general it can be said that myeloceles are inoperable; operation is indicated in meningoceles and in meningomyeloceles with evidence of only minimal neurologic involvement. The size of the deformity may preclude operation. Flaccid paresis of the lower limbs and coexistent hydrocephalus are contraindications to surgery. Seeping of meconium from a patulous anus together with dribbling of urine on gentle pressure of the abdomen is suggestive of impaired neurosphincter control. Hydrocephalus sometimes develops after operation and in the majority of cases is attributable to the coexistence of an Arnold-Chiari malformation. Congenital hydrocephalus may undergo spontaneous arrest. If arrest occurs within the first few weeks or months of life,

subsequent physical and mental development may be, and often is, unimpaired. In the absence of arrest, physical handicap is inevitable and mental retardation is usual. Death after a distressing closing phase customarily supervenes before the age of 5 years. The prognosis in microcephaly is consistently poor. Intellectual handicap is invariable and usually severe; convulsions are a feature of many cases; and eventually there is the problem of abnormal restlessness, aggressive behavior, or physical incapacity.

Detectable anomalies of the urinary tract present special problems in prognosis. Exstrophy of the bladder is not necessarily incompatible with life. When the malformation is only partial, plastic measures give good results. When the exstrophy is complete, moderate results are possible. When the ureteral orifices have been transplanted in the colon, distressing symptoms are likely to arise from metabolic disturbance due to the alimentary absorption of urinary chlorides. Operation is usually delayed until early childhood, and prognosis depends on continuing renal adequacy. Subsequent prolonged training is essential to offset difficulties in excretory control. There is no radical treatment for polycystic kidneys, which may give rise to death in infancy, childhood, or later life, depending on the amount of normally functioning renal tissue.

With regard to alimentary anomalies requiring surgical intervention, mention has already been made of general prognostic considerations. Operation within 12 hours of birth is indicated for exomphalos. Rupture of the peritoneal sac involves grave risk of fatal peritonitis; in the absence of this, 50 per cent of infants survive. Operative problems are greatest when the herniated viscera include the liver. Final complete closure may involve a second operation in the course of 10 to 14 days.

Abdominal obstruction may arise as a result of meconium ileus; stenosis, atresia, or malrotation of the gut; or Hirschsprung's disease. High obstruction is associated with a slightly better outlook, but preoperative prognosis should not attach value to clinical signs suggestive of the site of obstruction. All signs are fallible, often when least expected, and the frequent finding of multiple anomalies cannot be foretold. Operation is tolerated better in the first 48 hours than later in the first week of life.

The results of plastic operative measures for imperforate anus depend largely on the presence or absence of other malformations. Surgery may be performed in one or two stages. A rectovesical fistula involves risk of a chronic urinary infection. Prolonged training in later childhood is required in cases where sphincter control is absent or where recourse has been made to a permanent colostomy. Meconium ileus may resolve spontaneously or perforation of the intestine may occur; diagnosis is far from easy, and the need for surgical intervention may arise at any time. In any circumstances the condition is one of the utmost gravity. When obstruction is the result of Hirschsprung's disease, a colostomy gives immediate relief. Rectosigmoidectomy performed at a time of election in later infancy holds out reasonable prospects of cure.

Expert operative treatment of esophageal atresia is associated with a mortality rate of approximately 50 per cent. Success largely depends on there having been no aspiration of material into the lungs before operation. Excessive secretion in the

buccopharynx and "choking" at the time of the first feed should always arouse suspicion. A mucopurulent secretion of the nose is not infrequent. There is often a history of maternal hydramnios. Pyloric stenosis is uncommon in the first 10 days of life. Ramstedt's operation, performed without delay, is followed by the disappearance of symptoms. In experienced hands the mortality rate does not exceed 1 per cent. Hiatus hernia can simulate pyloric stenosis in the neonatal period. Response to medical treatment is often complete; operation is occasionally necessary in patients in whom symptoms persisting over months are associated with esophagoscopic evidences of esophagitis. The purpose of operation is to minimize the risk of stricture formation.

Obstructive jaundice may become evident toward the end of the first month. Medical trial of hydrocholeretic drugs for several weeks can be of value in excluding biliary occlusion due to inspissated bile, sometimes encountered in infants recovering from hemolytic disease. Signs of persistent obstruction are an indication for exploratory laparotomy. Operable biliary atresia is found in approximately 10 per cent of infants in these circumstances.

Two conditions require mention in conclusion. Hemorrhagic disease that has been promptly recognized and treated rarely results in death. If transfer to the hospital is decided upon, it should always be preceded by vitamin K therapy and precautions to counteract shock. Hemolytic disease is a complicated subject, but it can be said that of affected live-born infants, (a) approximately 95 per cent survive when effective arrangements are available for exchange transfusions to be given in the presence of accepted indications and reliable laboratory findings and (b) less than 5 per cent develop kernicterus, which commonly results in death; in the event of survival, physical and mental handicap is probable.

Any opinion given to parents concerning prognosis must take into account the facilities and services that are intended to be used. Standards vary enormously from locality to locality as they do from country to country. For this reason, detailed reference has not been made to the recorded results of different pediatric centers. With the continuing progress being made in nursing, surgical, and medical care of the neonate, these variations will lessen, and standards throughout the world will improve. Simultaneously, prognosis generally will become increasingly more favorable.

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Experimental Production of Congenital Malformations

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Twenty years ago only a few reliable experiments could be cited as proof that adverse environmental conditions can lead to congenital malformations in mammals. Although a wealth of experimental evidence was available that showed environmental teratogenic effects in lower animals, the mammalian embryo was thought to be so well protected in the maternal uterus that prenatal malformations were not attributed to external influences. In the last 20 years many well-controlled experiments in mammals have demonstrated that congenital malformations can be induced in the offspring of mothers subjected to various adverse environmental conditions. Such conditions, especially created by the experimenter for this purpose, are usually so different from natural conditions occurring in human pregnancies that physicians may ask whether artificial experiments of this type give any information concerning the causation of congenital malformations in man.

Severe congenital defects have been induced by deprivation of the mother of essential nutrients or oxygen, by administration of antagonists or toxic substances, by injection of dyes, by roentgen-ray irradiation, and by other teratogenic procedures. Some of these experiments were better controlled than others; some were performed in stocks with little tendency to spontaneous malformations, others in breeds exhibiting marked spontaneous variations; some have been repeated in various laboratories, others still require confirmation; some of the investigations were reported as factual animal experiments, others as representative of human conditions. In many instances, the interpretations were not made by the investigator but by persons not acquainted with the details of the study. It is difficult therefore for the casual reader to evaluate and interpret the experimental evidence.

In order to appreciate the value of teratologic experiments in mammals, one must consider them in historical perspective.

Three decades ago, one could find many statements in the literature asserting that all congenital malformations in man are genetically determined and hereditary. It was conceded that mechanical interference by amniotic bands or abnormal pressure could be responsible for rare malformations such as amputations, but it appeared doubtful that internal, systemic, symmetric, or familial congenital defects could be due to other than genetic factors. Since a great deal was known about the heredity of congenital defects in man and in animals, most congenital malformations were, in the absence of other known causes, attributed to heredity. This conception was not without practical consequences. In 1935, for instance, an author found familial occurrence of harelip and cleft palate in 20 per cent of his patients with cleft formation. Since no other than genetic causative factors for cleft formations were known at that time, he considered the remaining 80 per cent also hereditary and recom-

mended that all patients with cleft palate be sterilized! Such radical attitudes were not rare at that time, particularly among geneticists in Germany. It was of interest therefore that between 1935 and 1945 several methods were developed making possible the production of internal, systemic, and even "familial" malformations by maternal vitamin deficiencies. These experiments were important not because they showed that maternal dietary deficiencies induce malformations, but because they demonstrated beyond any doubt that the mammalian embryo may be structurally damaged and deformed by rather subtle environmental forces. This concept was borne out when in 1940 Gregg discovered that German measles of the mother could result in congenital defects of the embryo. It became apparent that environmental factors could cause malformations not only in experimental animals but also in man. Subsequently it has become generally accepted that environmental as well as genetic factors must be considered in etiologic studies of human malformations. Furthermore it has been recognized that congenital defects, such as microcephaly, cataract, cleft palate, syndactylism, and others, may be hereditary in some cases and nonhereditary in others. The imitation of a genetically determined malformation by a nonhereditary one has been called a "phenocopy." Geneticists are now aware of the necessity of excluding phenocopies from their studies of hereditary defects. It is obvious that eugenic prognoses differ in families with genetically determined defects from those in families in which a phenocopy occurs. Recognition of the complex causation of malformations has for the time being complicated eugenic prognoses immensely, but it is better to realize that we have no simple answers to the complicated questions involved in eugenic prognosis and counseling than to give unfounded advice.

Thus animal experiments have established the possible role of environmental factors in the etiology of congenital malformations, but animal experiments have also aided greatly in the understanding of malformations of genetic origin. For many years, geneticists have studied inbred strains of mice and of other mammals and found hereditary congenital defects in some of them. In many instances it could be demonstrated that such defects are inherited as simple Mendelian traits. Other defects behave differently. Although the anomalies appear and reappear in certain strains, they cannot be obtained with the regularity to be expected in simple Mendelian inheritance. Many of these irregularities could be attributed after careful observation and experimentation to genetic complications; others must be explained by nongenetic chance factors. Thus it appears that even in inbred strains some malformations are due to a combination of genetic and nongenetic factors. Inbred strains have also been used in experiments designed to produce malformations by environmental influences. Such experiments have clearly demonstrated that different strains react differently to similar environmental factors. While in some strains malformations can be produced by a certain injurious procedure, other strains are immune to the same injury. It must be assumed therefore that many congenital malformations are due to both genetic and environmental influences. We are far from understanding the complicated interplay of such factors in the etiology of most congenital malformations in man. Thus animal experiments have taught us—if nothing else—that great caution must be exercised at present in the interpretation of human mal-

formations and that much work needs to be done in the future to elucidate the etiology of prenatal defects.

Animal experiments can be used not only in etiologic research, but also in investigations of the pathogenesis of congenital malformations. Since the development of prenatal defects is not accessible to direct observation in man, teratologic experiments in mammals can contribute greatly to a better understanding of the mechanisms leading to congenital structural errors. The geneticist who discovers a congenital malformation regularly in an inbred strain of mice can trace backwards the development of the defect by examination of embryos of different ages. In this way the earliest deviations from normal organogenesis can be discovered and the pathologic processes resulting in specific malformations studied. Developmental genetics is a well-developed science that contributes greatly to our understanding of the processes resulting in abnormal structures. Similarly, embryologic studies can be made in the young of animals subjected to experimental teratogenic procedures. Thus the pathogenesis of ocular defects, hydrocephalus, spina bifida, cleft palate, horseshoe kidney, or hydronephrosis can now be followed and studied in planned animal experiments. A wealth of material is available for such analyses and it should replace the speculations and theories offered in the past on the morphogenesis of congenital malformations.

There are several conclusions to be drawn by the physician from teratologic animal experiments. Congenital malformations may be determined before conception by genetic mechanisms or they may be determined by environmental factors between conception and birth. The latter type is not hereditary. The relative importance of the two mechanisms for the malformations occurring in children remains to be established and cannot be evaluated satisfactorily at this time. The difficulties of recognizing which mechanism is involved in a given case are intensified by the fact that genetic weaknesses can be transformed into malformations by environmental factors, thus placing responsibility for a malformation upon a combination of circumstances. In addition, the physician must remember that a hereditary malformation may be imitated by a nonhereditary phenocopy. It is sometimes possible to distinguish between hereditary and nonhereditary defects by a careful analysis of the family history and of the history of the pregnancy resulting in the abnormal child. However, in most instances eugenic prognoses should and must be guarded. The physician interested in the morphogenesis of certain congenital malformations should know that experimental methods are available permitting embryologic studies of many deviations from normal development, and that theories about the pathogenesis of many prenatal malformations can now be tested by observation of their development in mammals.

Psychochemotherapy of Mental Deficiency in Children

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I. EXPERIMENTAL STUDIES

Mechanism of Action of Psychochemotherapeutic Agents. The mechanism of action of the newer psychochemotherapeutic agents is as varied as the propounders. Marrazzi[20] suggests interference with blockage or stimulation of adrenergic or cholinergic systems altering the normal equilibrium level of transmitters. Grenell[9] considers certain structural differences in receptors more determining than the trigger mechanisms in the network of responses. Rosenberg[27] attributes drug action to their differing effects on the ascending reticular activating system. Many cell groups of the brain react differently according to the various parameters of response based on specific physicochemical changes. Grenell[9] demonstrated changes in activity of selected cell groups and in the primary action of specific drugs on cerebral areas reflected by their response to stimulation.

The crucial problem in mechanism of action is concerned with the structure of neuronal membranes in different areas of the brain and their relationship to the specific properties of the molecules with which they react. Mullins[22] found that the excitatory action of each drug produces a local disorder in the oriented molecular structure of the cell membrane. The reorientation of particular molecules confirms this concept; for example, one isomer of hexachlorocyclohexane acts as a narcotic while another isomer acts as a convulsant. The slightest reorientation of reserpine destroys its tranquilizing or antagonizing action to serotonin. Grenell[9] found local selectivity of psychochemotherapeutic agents basic to the effects produced as a result of deviation from the normal regional interaction of several levels of the central nervous system.

The biochemical concepts of the action of psychochemotherapeutic agents are thus delimited by our understanding of brain function in health and disease. The mesodiencephalic activating system is aroused by stimulant drugs such as amphetamine and is depressed by the barbiturates. Small doses of chlorpromazine block the arousal reaction, but large doses of chlorpromazine and small doses of reserpine arouse the activating system. Nevertheless, both drugs depress the hypothalamic centers controlling basal metabolism, temperature, blood pressure, and the wake-sleep cycle. The depression of the hypothalamus by reserpine is balanced by its stimulation of the activating system, the end result being wakeful sedation, whereas chlorpromazine depresses the activating system. Reserpine is a potent tranquilizer, but chlorpromazine has more deep-seated effects. Each functions specifically without any demonstrable synergism between them. Development of depressive manifestations following prolonged reserpine therapy may be reversed by elimination of the drug, but development of jaundice following prolonged chlorpromazine adminis-

tration does not preclude its subsequent administration without further complications.

Lysergic acid diethylamide has marked effects on cerebral circulation. Minute doses produce striking aberrations in psychologic and mental function. In vitro studies of cerebral metabolism suggest alteration in cerebral oxygen utilization, its antagonism to the effects of serotonin implying an alteration in cerebral circulation. But Sokoloff[32] observed no changes in cerebral blood flow, vascular resistance, oxygen consumption, glucose utilization, or respiration quotient following intravenous administration of 120 μg. of LSD in normal and mentally disturbed patients. Apparently, psychologic alterations produced by LSD are not associated with any changes in cerebral circulation or in gross oxygen and glucose utilization by the brain.

Compounds with a diphenyl nucleus inhibit cytochrome oxidase activity and oxidative phosphorylation in brain mitochondria. Chlorpromazine with a phenothiazine molecule is structurally similar to the diphenyl compounds and is an effective inhibitor. Related compounds with several aromatic groups such as naphthyls and phenanthrenes are also marked inhibitors. Abood[1] found reserpine, methylene blue, phenyl ether, and β-naphthol to produce inhibition, and SKF 501, a structural analogue of chlorpromazine, more deep-seated inhibition without affecting the cerebellum or cerebrum. Apparently, psychochemotherapeutic agents act on coenzyme I-linked phosphorylation and at the electron transfer level involving oxidation of ferrocytochrome C.

Psychochemotherapeutic agents alter the transmission equilibrium and consequently mental function. Marrazzi[20] found that serotonin, which is endogenous to the brain and related to adrenalin, is a potent cerebral neurohumoral inhibitor. Psychomimetic drugs, structurally related to adrenalin or its oxidation product, produce synaptic inhibition that can be prevented by prophylactic doses of tranquilizers such as chlorpromazine, reserpine, and azacyclonol in amounts that in themselves do not alter synaptic transmission.

Serotonin is a simple, hormone-like compound indispensable in the function of the autonomic and central nervous systems. Rapport[26] crystallized, named, and deduced the structure of the compound as 5-hydroxytryptamine, which Hamlin et al[10] and Erspamer[6] found identical to synthetic preparations. Serotonin occurs in the stellate ganglia, released by stimulation of certain peripheral nerves and antagonized by endogenous or exogenous compounds that induce mental disorders. Woolley and Shaw[36] found that serotonin plays a determining role in the central nervous system by maintaining normal mental processes, since antimetabolites that interfere with serotonin action produce specific interference with brain function simulating schizophrenia. Serotonin deficiency in the brain is thus brought about by failure of the metabolic processes that normally synthesize or destroy hormones. Since serotonin does not penetrate the brain following peripheral administration, serotonin-like compounds are being tested.

Udenfriend[35] demonstrated that tryptophan is the dietary precursor of serotonin, being hydroxylated to 5-hydroxytryptophan and then specifically decarboxylated to serotonin. Monamine oxidase destroys serotonin by oxidation to 5-hydroxyindolacetic acid. Both serotonin and monamine oxidase are localized in the hypothalamus

and other primitive portions of the brain where serotonin is synthesized for specific mental functions. Pyridoxine deficiency diminishes serotonin formation dependent on pyridoxal phosphate decarboxylase. Administration of iproniazid, the monamine oxidase inhibitor, increases brain serotonin threefold. Furthermore, 5-HTP, the amino acid precursor of serotonin, is rapidly converted to serotonin wherever the specific enzyme 5-HTP decarboxylase occurs. It is thus possible to increase the amount of brain serotonin in studying its effects on the central nervous system. Axelrod[4] found that chlorpromazine, serotonin, and reserpine inhibit metabolism of LSD by the microsomal preparation 70, 40, and 20 per cent, respectively.

Comparative Effectiveness of Psychochemotherapeutic Agents. Studies of mentally retarded children reveal every type of behavior or personality disturbance. The author[18] unraveled their abnormality not only by their failure to develop normal biologic reactions but also by their tendency to abnormal reactions arising spontaneously or induced by unsuspected stress. Our first approach in this study of aments' reactions was to determine the underlying basis of their aberrations, selecting appropriate cases with paired controls before testing the relative effectiveness of the newer psychochemotherapeutic agents in individualized and institutional practice. The heterogeneity of presenting problems veered this study toward single symptoms or specific manifestations in all types of amentia for this five year study.

Psychochemotherapeutic agents were given orally before feedings and gradually increased or decreased at 48 hour intervals according to definite indications and individual tolerance. Each compound was tested for a fortnight and an equivalent supplemented or reinforced depending on the type of response. Children showing clinical improvement were given maintenance doses for six months, while those who failed to show any improvement were shifted to different preparations. Each group of retarded children was selected for predominant symptomatology in alimentary, motor, and emotional behavior and sleep disturbances as a basis for the therapeutic evaluation of 10 drugs in terms of degrees of alleviation of 25 single symptoms in 240 retarded children affected by six groups of behavior disturbances.

Quantitative comparisons between psychochemotherapeutic agents required calculating means, standard deviations, and standard errors in some of the assessments of behavior disorders amenable to measurement, such as caloric intake in excessive appetite or distance covered in hyperactivity, but qualitative statistics did not lend themselves to such numerical refinements. In appraising large samples, differences greater than three times the standard error were significant, but in small samples, the rule of three does not necessarily maintain unless the number of cases exceeds 15.

Alimentary disorders differ markedly in the ament from those in the normal child, more often due to emotional than to physical factors. Excessive appetite was curtailed by amphetamine in 14 cases and by chlorpromazine in 16 cases out of 28. Pica was reduced somewhat better by chlorpromazine than by reserpine (Serpasil*) in 8 children. Psychogenic vomiting was relieved in more than one-half by chlorpromazine and in less than one-half by meprobamate (Equanil†) in 18 children.

* The trade name of Ciba Pharmaceutical Products, Inc., for reserpine is Serpasil.

† The trade name of Wyeth, Inc., for meprobamate is Equanil; the trade name of Wallace Laboratories, Inc., for meprobamate is Miltown.

Body manipulations carried out at high levels of consciousness, performed continuously for years, remained under voluntary control as pleasurable habits. Thumb-sucking responded best to diphenhydramine hydrochloride (Benadryl*) in 24 children, lip sucking to chlorpromazine, and nail biting to meprobamate (Equanil). The results were not striking, yet one third of the group were halted in habitual manipulations of the face, actions that made the child's mental defect more obvious. A similar therapeutic approach to halt the handling of the genitals was without avail.

Motor disorders are bizarre in aments in comparison with those observed in normal children, since the lack of proper coordination and the clumsiness and awkwardness are symptoms of motor infantilism distinct from any defects in the motor apparatus. Whatever the motor defect or disturbance, the movements are greatly accentuated when the child is upset, and completely attenuated when the body is at rest. Restlessness was alleviated in about one half of the 50 children observed by continuous administration of reserpine and chlorpromazine. Head banging was diminished in less than one-half the children with massive doses of chlorpromazine and meprobamate (Miltown). Tics involving the head, eyes, face, and shoulders were alleviated in 24 of 36 children by methylphenidylacetate hydrochloride (Ritalin†), chlorpromazine, and meprobamate (Equanil). Hyperactivity, so characteristic of the moderate or severe young ament, was fortunately amenable to considerable control with reserpine, diphenhydramine hydrochloride, meprobamate (Miltown), and chlorpromazine in 38 of the 67 children.

Emotional disorders are deep-seated and rarely amenable to medical measures in the young ament. Temper displays accompanying severe emotional upsets were diminished in about one half of the 32 children by reserpine and chlorpromazine. Breath-holding attacks, in which some children become cyanotic and even unconscious, were alleviated in only one third of the 18 children susceptible to these seizures devoid of any epileptic components. Phobias and fears more prevalent in mildly retarded than in severe aments were cleared in 12 of the 25 children by chlorpromazine and meprobamate (Equanil). Anxiety symptoms produced by situations frightening to the ament were diminished in about one half the 60 children by reserpine, chlorpromazine, and meprobamate (Equanil).

Behavior disorders are individual in pattern and persistent in performance according to the degree of amentia. Negativism was attenuated but not eliminated in one third of the 20 children observed. Aggression as a fundamental component of the child's emotional make-up is invariable because of the failure to canalize aggressive potential. It was diminished by one-half in these cases with reserpine and chlorpromazine, but the cruelty to younger children or animals based on a feeling of inadequacy and repression persisted despite massive doses of chlorpromazine. Destructiveness was moderated but not eliminated in one third of the 17 children observed.

Sleep disorders are more prevalent among the mildly retarded than the severely

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* The trade name of Parke, Davis & Co. for diphenhydramine hydrochloride is Benadryl.

† The trade name of Ciba Pharmaceutical Products, Inc., for methylphenidylacetate hydrochloride is Ritalin.

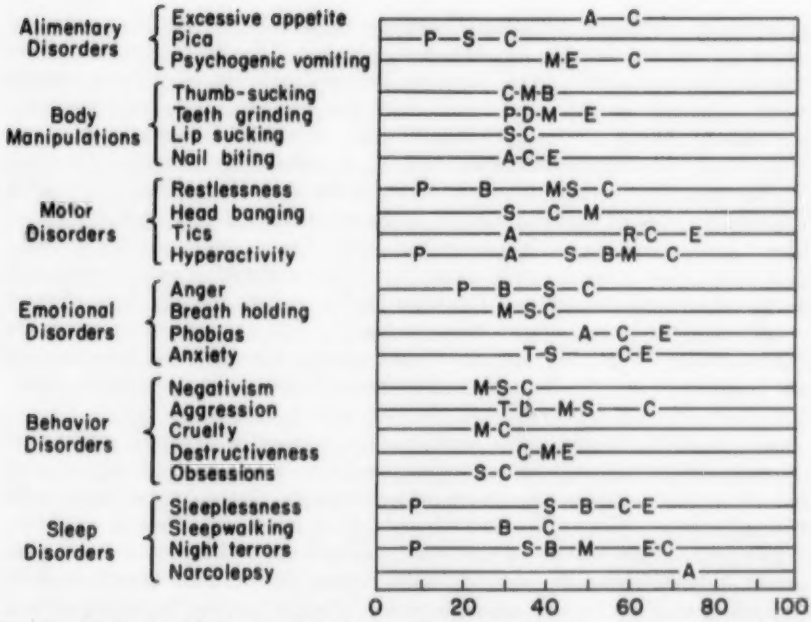

FIG. 1. Comparative effectiveness of psychochemotherapeutic agents in amentia symptomatology of children. Code A = amphetamine; B = Benadryl (diphenhydramine hydrochloride); C = chlorpromazine; D = Dilantin (diphenylhydantoin sodium); E = Equanil (meprobamate); M = Miltown (meprobamate); P = phenobarbital; R = Ritalin (methylphenidylacetate hydrochloride); S = Serpasil (reserpine); T = Tolserol (mephenesin).

retarded aments. Most find a familiar ritual at bedtime essential for their peace of mind and cannot readily fall asleep if it is broken. Sleeplessness responded to reserpine, diphenhydramine hydrochloride, chlorpromazine, and meprobamate (Equanil) in one-half the children, while phenobarbital merely enhanced bedtime excitement. Hexobarbital sodium (Evipal*) is the only barbiturate that relaxes rather than stimulates the ament, but the psychochemotherapeutic agents produce a prelude of relaxation conducive to undisturbed sleep. Nightmares or night terrors, manifestations of anxiety emanating from some particularly frightening experience, are not unusual in the disturbed ament, and were responsive in half the cases to meprobamate (Equanil) and chlorpromazine. But narcolepsy responded to amphetamine in 6 of 9 children, while sleepwalking was not much altered by any form of therapy.

Figure 1 indicates the relative merits of each of these drugs used in sequence on the groups of children studied, ranging from 10 to 50 per symptom. The line scales give the percentile improvement of symptoms by the drugs evaluated. These psychochemotherapeutic agents merely shield the body from reflex disorders emanating from pathologic focal sites in the brain and nervous system. They suppress the overt

* The trade name of Winthrop-Stearns, Inc., for hexobarbital sodium is Evipal.

manifestations without eliminating the underlying pathology. The drugs interfere with the tissue reaction to the abnormal process but do little to accelerate its elimination from the body. They serve the purpose, therefore, of reducing internal discord and maintaining the child in an improved state while the body gradually overcomes or compensates for its dysequilibrium. Withdrawal of the drugs merely reproduces the original manifestations without any untoward symptoms. All previous aberrations are reversed without affecting the underlying cause. The most effective agent cleared the symptoms in only two thirds of the cases, and the least effective agent barely altered the symptomatology. The chemical basis for effectiveness is determined by the degree of reactivity of each of the drugs upon the reticular substance activating the cortex. The more binding the reactor, the more effective the agent and the more dangerous the side effects. The least active agents are not without danger, because of their cumulative effects. Consequently, great caution must be exercised in individualizing psychochemotherapeutic agents from the standpoint of positive and negative effects, clinically and chemically.

Psychochemotherapeutic agents reinforce their activity in geometric rather than arithmetic progression. The effect is rarely additive, for each structural grouping produces its own addition-compound formation with the chemical constituents of the brain and nervous system. We have observed no simple additive effects exerted by reserpine and chlorpromazine or any other combinations of different chemical composition. Of the two compounds the latter is more potent, more immediate in its effectiveness than the former, and more toxic. The dosage must be individualized, the weaker compounds requiring higher dosages than the more reactive compounds. But if a child is responsive, a relatively smaller dosage will be effective in a matter of weeks in acute cases and of months in chronic disorders. The different levels indicated for meprobamate (Miltown) and meprobamate (Equanil), both of the same chemical composition, are based on the prolonged use of the latter after the former has become unavailable.

II. CLINICAL APPLICATIONS

Treatment of Intellectual Impairment. Thyroid, desiccated, exercises striking physiologic and pharmacologic effects. Thyroxin or thyroglobulin has no special advantage. The hormone increases mental acuity, overcomes mental obtundity, and corrects psychomotor retardation in the ament with substandard metabolic rate. Ross et al[28] observed an acceleration of cortical alpha rhythms, Cohen and Girard[6] an increased rate of oxidation of brain tissue, indicating a rise in cerebral metabolism. I observed that the intelligence quotients of young hypothyroid aments increase during the first year of thyroid treatment and the aments retain these mental levels on maintenance doses of thyroid. Desiccated thyroid is administered orally, 0.5 gr. daily for each year up to 6 years and 1 gr. or 1.5 daily thereafter. The dosage is increased from time to time by 0.25 gr. increments until the optimum therapeutic effect has been attained without exceeding tolerance. The ament becomes active mentally and energetic physically.

Excessive therapy revealed by excitability, nervousness, hyperactivity, irritability,

behavior disorders, tachycardia, sweating, and weight loss calls for diminution or elimination of thyroid or, preferably, a single dose once a week. Thyroid therapy accelerates the ament's growth and development, which tend to lag behind the normal. Optimal dosage is estimated from height, chronologic age, and bone age. The euthyroid ament tolerates thyroid better than the hypothyroid ament but tends to develop susceptibility to infection, nervousness, emotional instability, and sleeplessness. Discontinuance of the thyroid for a week with reinstitution at a lower dosage eliminates untoward manifestations.

Glutamic acid is a nonessential amino acid abundant in an adequate diet. Nachmansohn et al[23] observed its role in the enzymic synthesis of acetylcholine in cerebral metabolism. Price et al[24] found that the compound increases mental power. Zimmerman and Ross[37] confirmed this property by increasing the learning ability of white rats with glutamic acid. Albert et al[2] observed a rise in I. Q. in 7 of 8 mentally defective persons. Zimmerman and Ross[35] recorded an average rise of 10.8 in I. Q. during the first six months, and less thereafter, in 30 aments with I. Q.'s exceeding 50. The best results were obtained with children devoid of cerebral damage and behavior disorders. Quinn and Durling[26] found that glutamic acid stimulates mental and physical activity in certain aments. But McCulloch[19] observed no mental improvement in any ament. Heim and Wallace[11] attributed the rise in I. Q. to repeated testing by the same procedures. In my practice I find the optimal effect of glutamic acid statistically significant in mild and moderate aments free from bizarre behavior. But in unselected cases, purposeless activity becomes greatly accelerated and the ament's behavior uncontrollable. In addition, recurrent acidosis during mild infections reflects an unstable acid-base mechanism disturbed by large doses of glutamic acid.

Thiamine is the antineuritic vitamin indispensable in cerebral metabolism. Himwich[12] found subnormal oxygen utilization in malnourished aments. Since mental function depends on thiamine for oxidation of dextrose, the vitamin has been reinforced in the ament. Spies[33] observed striking changes in the electroencephalogram after thiamine therapy in frank deficiency. Others correlated disturbances of the higher nerve centers, i.e., forgetfulness, difficulty in orderly thinking, poor performance in school, vague fears, and irritability, with inadequate thiamine intake for normal tissue respiration. Rudolf[29] observed improvement in behavior in some aments, a rise in social quotients in some, and uncontrolled behavior in others. Thiamine stimulates neuronic activity but cannot supply intelligence or common sense. Excessive stimulation of lower neurons merely increases undesirable activity. I have never observed any mental or scholastic improvement on thiamine therapy except in the malnourished, institutionalized ament.

Amphetamine sulfate (Benzedrine*) and dextro amphetamine sulfate (Dexedrine†) give the disturbed child a feeling of well-being in a wide variety of behavior disorders, i.e., psychologic, convulsive, nervous, schizoid, and postencephalitic. The drugs have a favorable effect on fear, depression hyperactivity, and sexual tension

* The trade name of Smith, Kline & French Laboratories for amphetamine sulfate is Benzedrine.

† The trade name of Smith, Kline & French Laboratories for dextro amphetamine sulfate is Dexedrine.

and an unfavorable effect on severe amentia, schizophrenia, and psychopathic states. Amphetamine sulfate subdues the child but stimulates the adult. An ament becomes less active, less noisy, and less difficult. He shows quicker mental responses, greater attention span, better cooperative effort. There may, however, be unfavorable effects from amphetamine sulfate, such as anorexia, irritability, seclusiveness, and sleeplessness. Administration of amphetamine sulfate in 20 mg. and dextro amphetamine sulfate in 10 mg. doses daily is usually effective; otherwise, either compound may be gradually increased until a therapeutic effect is obtained. The daily quota is divided into two doses, given before breakfast and before noon. The resultant effects observed within one-half hour are maintained for about five hours. Overdosage first causes restlessness, talkativeness, irritability, and insomnia, and then confusion, delirium, convulsions, and coma.

Diphenylhydantoin sodium (Dilantin*) is effective in behavior disorders associated with electroencephalographic changes resembling epilepsy, especially irritability, hypermotility, and variability of behavior. It is a stimulant rather than a sedative drug. A young child requires 0.5 gr. three times daily, mixed with cream to disguise the bitter taste and to diminish gastrointestinal irritation. The older child requires about 1.5 gr. three times a day given in capsules. Diphenylhydantoin sodium does not have the hypnotic properties of phenobarbiturates. Hyperplastic reactions of the gums may be overcome by ascorbic acid, but other toxic manifestations require discontinuance of the drug. Paraldehyde has a calming effect on an ament in a state of high excitement. It may be given rectally, 1 teaspoonful in 1 oz. of oil by retention enema or intravenously if necessary.

Mephenesin (Tolserol†) is a muscle relaxant in spastic disorders involving the region of the thalamus, internal capsule, cortical nuclei, or brain stem. It provides a state of relaxation with a pleasant feeling of warmth, numbness, and euphoria for two to three hours. Muscle spasm, spasticity, rigidity, tremor, and startle often disappear, and the child is able to fall asleep normally during the effective period. The usual dose ranges from 0.75 to 1.5 Gm. daily.

Dibenamine blocks excitatory sympathetic responses without disturbing the inhibitory effects. It is a synthetic nitrogen mustard derivative too costly to be administered by any other method than dilute intravenous drip of 2 to 3 mg./Kg. in 500 cc. saline in one hour. Unfortunately, the number of side reactions, such as mental confusion, visual impairment, nausea and vomiting, and loss of bladder control, limits its usefulness. Insulin in subshock dosage is produced by hypodermic injection of regular insulin beginning with 5 units daily and increasing by 5 units until the precomatose stage of classic insulin therapy is attained. After about 30 units, the child manifests hunger followed by fall in body temperature, salivation, and increased perspiration. The injections are given daily for two or three weeks and the insulin dosage gradually reduced.

Niacin improves depressed states by its vasodilatory effects. Preferred to the amide because of this effect, it is given in 25 mg. tablets 15 minutes before each meal. If

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* The trade name of Parke, Davis & Co. for diphenylhydantoin sodium is Dilantin.

† The trade name of E. R. Squibb & Sons, Inc., for mephenesin is Tolserol.

there is no untoward reaction, the dose is increased to two and eventually to three tablets before meals, maintained for a week, and then gradually reduced until improvement.

Treatment of Motor Disturbances. Hyperactivity is a motor agitation accompanied by nervousness, restlessness, and fidgetiness. It indicates lack of satisfaction from any activity undertaken or reflects an unstable nervous system unable to withstand the strain of everyday life. The ament's responses to stimuli are exaggerated because his inhibitory powers are decreased. His compulsive agitation impairs his capacity for purposeful activity. He feels uneasy about his surroundings, uncertain of his abilities, and apprehensive of his elders. He lacks the complex integration essential for regulated behavior.

Continuous overactivity induces a ravenous appetite comparable to the behavior of animals with induced frontal lobe lesions. Some ascribe this motor unrest to a surplus of inner compulsions originating in the brain stem. This "organic driveness" is characterized by marked overactivity with choreiform or ticlike movements, difficulty in maintaining momentary calmness, clumsiness in performances and movements, and explosive motor release of all voluntarily inhibited activity.

Evaluation of the ament will determine the underlying basis of his overactivity, nervousness, and fatigue. If mental or physical, adequate outlets for satisfying play and motor activity should be obtained in a nursery or special school, indoors and outdoors, to release tension. If emotional, the anxiety will be overcome by play therapy or psychotherapy. If epileptic, individualized drug therapy will be effective. Parents must strike a balance between rigid routine, which constricts these souls, or no routine, which leaves them anxiously bobbing about. Sedatives are invaluable adjuvants of the fundamental therapy in effecting a pattern that will become self-perpetuating.

Head banging, head rolling, and bed rocking develop during the transition in locomotor development. These motor habits predominate in children with innate rhythmic ability to relieve tension and anxiety. The movements may continue for hours to satisfy a basic need for rhythm. The habit must be distinguished from spasmus nutans in infants reared in a dark room or afflicted with visual defects and from salaam spasm occurring in organic brain disease or epilepsy. Treatment in the form of mechanical restraints or substitution therapy is of no avail. Some use rhythmic auditory stimulus such as a metronome to satisfy the child's rhythmic sensations at bedtime. Special rhythmic movements are introduced into the ament's play, by means of hobbyhorse, seesaws, music, and dancing.

Tics or habit spasms are sudden, rapid involuntary movements of circumscribed muscle grasps. The face and neck are more frequently involved, but almost any part of the body may participate. There may be blinking, grimacing, coughing, throat clearing, sniffling, swallowing, hiccoughing, shoulder jerking, or trunk movements. Tics predominate in emotionally disturbed boys with an I. Q. above 50, but rarely occur in children with an I. Q. below 50. Treatment must be directed at the underlying emotional difficulty by improving the child's adjustment at home, at play, and at school. Parental admonition, nagging, and criticism are of no avail.

Temper tantrums occur in the young ament prevented from doing what he wants to

do or made to do what he refuses to do. Actually, the child is trying to get what he wants or needs and does not know a better way of getting it. Sometimes, displays of temper are an effective means of getting his own way. Attacks may indicate negativism, hostility, emotional upset, or parental imitation. The child should be calmed and taught that he cannot get his way by such methods. If such behavior occurs publicly, he should be soothed and taken home. The more casual the attitude, the easier it is to manage the attack. The child must be made to realize that he will not get his way with tantrums. He should be put into a safe room to calm down without injuring himself or destroying property.

Treatment of Body Manipulations. Thumb-sucking satisfies an innate sucking drive in the placid ament, a by-product of the gratification of hunger and thirst. The mouth remains a source of pleasurable satisfaction throughout life from finger and object sucking in infancy to nail biting and gum chewing in childhood and munching and smoking in adulthood. The habit of sucking the thumb, finger, or tongue is a normal relief from discomfort and loneliness in infancy, a manifestation of boredom and frustration in early childhood, and of some personality disorder in late childhood.

Treatment involves correction of the total situation rather than of the bad habit. Mechanical restraints, bitter compounds, tape, teasing, and threatening are of no avail. The ament who feels unloved, unwanted, or upset will not give up the practice unless he gets something as pleasurable in return, i.e., parental love and warmth, understanding, and attention. The ament's hands should be kept busy in satisfying activities in ways appropriate to his interests and abilities.

Nail biting is an expression of tenseness in the excitable ament. The habit is practiced during repressed excitement or is copied from other members of the family. Threats, restraints, scoldings, and bitter drugs are of no avail. Treatment should be directed at the child to relieve the causes of his tension. Mittens worn at night will minimize fingernail biting, and pajamas covering the feet will minimize toenail biting. Easing the tension paves the way for building self-confidence and security by eliminating the pernicious habit with the child's cooperation.

Nose picking may be associated with putting the contents into the mouth. Early training in the use of a handkerchief may prevent the development of the habit. Appealing to the ament to refrain from this unpleasantness may be effective. *Lip biting* is often associated with lip sucking following emotional distress. Lubricating the dry, cracked lips with petrolatum and appealing to the child's pride may minimize the practice. Teeth grinding during daytime and sleeping hours enables the ament to release bound tensions. It may become an attention-seeking device perpetuated by parental anxiety about the practice. Increasing the outgoing activities and easing everyday tensions will minimize the habit.

Masturbation accompanies other rhythmic manipulations of the ament body. It is a source of satisfaction to compensate for unhappiness, fatigue, or frustration. The practice provides a normal release from sexual tension with or without erotic stimulation. The ament finds masturbation a more satisfactory solace than autistic pleasures. The habit may become so persistent, with flushed face, fixed eyes, and bodily contortions, that a diagnosis of epilepsy is considered from the parental

history. Physical restraint is useful in early infancy. Amphetamine sulfate on arising and diphenhydramine hydrochloride at bedtime will decrease the tendency. Anesthetic ointment applied to the genitals is a useful adjuvant. Scolding, frightening, and punishing merely aggravate the condition. Parental attitudes should be corrected and fears allayed about the consequences.

Treatment of Alimentary Disorders. Anorexia may be congenital in the ament showing a decrease in digestive secretions. It is difficult to manage with concentrated feedings and supplements. Nevertheless, the child somehow progresses at a slow pace without parental anxiety or forcing. Anorexia is usually psychogenic when the difficulty pertains to certain foods. The ament likes some foods one day and refuses them the next day, according to mood. Such feeding behavior is often accompanied by allergic food finickiness, poor chewing, and unwillingness to swallow solid particles. Anorexia due to organic disease relates to all foods in the daily diet. The feeding difficulty is accompanied by apathy, fatigability, nervousness, and sleeplessness. Poor appetite may be observed from birth, the ament preferring sleeping to eating. Poor sucking reflex or absent hunger contractions may appear on an organic basis or poor chewing and hesitant swallowing on a genetic basis.

After infancy, anorexia usually accompanies the rapid psychologic development and slow physical growth. Forcing food to increase the gain in weight or competing with another child aggravates the difficulty. Feeding the ament after he is able to eat by himself usually creates psychologic problems that aggravate anorexia. Parental concern over food intake during acute illness may initiate poor eating habits as a means for gaining attention. More often, the feeding difficulty is but one of the many deep-seated emotional states such as excitement, tension, and unhappiness accompanying amentia.

Treatment depends on the underlying mechanism. The difficulty usually lies in the parents and not in the child. They should be advised about the decreased appetite and slow weight gain after the first year of life, about the futility of coaxing, distracting, bribing, threatening, forcing, punishing, or giving medication to the child. He should be given small amounts of a variety of foods for adequacy and a free choice of meat, fruit, ice cream, and milk in this sequence because of the usual distaste for vegetables. A pint of milk will meet the calcium needs, but forcing more milk will diminish appetite. Spicy and fried foods are preferred to the simple cooked foods. Each course should be prepared interestingly and served attractively, but no food should be given between meals.

An ament should learn to feed himself, to eat alone peacefully, and to have all food removed after half an hour without comment. Dawdling over food is a negativistic reaction to overauthority. If he eats slowly, chews weakly, and swallows sparingly, discontinuance of strained or mushy foods will enable him to adapt to solid foods that require chewing. He can be weaned from the infantile manner of feeding by giving him increasing opportunity for self-feeding. Later he should be allowed to help in the preparation of the meal to increase his appetite for products of his own handiwork.

Adolescent anorexia may produce severe malnutrition, especially in girls, as a result of emotional shock. The physical starvation parallels the emotional starva-

tion. There is marked loss of weight and strength, dehydration and acidosis, dryness of the hair and skin, brittleness of the nails, and the appearance of aging. The author[14] found the basal metabolic rate, blood sugar, blood pressure, and body temperature to be subnormal. Parenteral feeding in the hospital will correct the malnutrition, and psychotherapy in the convalescent period will correct the aversion to food.

Bulimia or excessive appetite is usually due to overindulgence or overactivity. It may be imitative of an excessive eater in the family or indicative of the mistaken notion that extra feeding improves the mind. More often, excessive appetite is an expression of deep anxiety in an emotionally disturbed ament. Food is the principal source of satisfaction. Shorvon et al[31] observed that eating relieves feelings of helplessness, compensates for other satisfactions, and gains parental approval. But excessive appetite may occur in lesions of the cerebral cortex, in tumors of the frontal lobe, in head injuries and lesions of the hypothalamus, such as encephalitis, chorea, and neoplasm.

Pica or perverted appetite is not uncommon in the ament. He may eat anything he can pick up, whether it be dirt, sand, plaster, wood, coal, chalk, or paper. He may pick fuzz from the blankets, chew paint from toys, or eat magazines. The effects of this habit depend on the composition of the foreign bodies ingested. If the child persists in eating paint, he may develop lead poisoning; if he indulges in pulling out and eating his own hair, he may develop intestinal obstruction; if he tends to eat feces, he probably shows schizophrenic manifestations rather than marked amentia. If he consumes foreign bodies in excess, the stomach becomes filled with a solid mass, giving rise to malnutrition, indigestion, fetor, vomiting, and obstruction.

The craving is unrelated to dietary deficiency or hypochromic anemia but is a manifestation of a personality disorder. A retarded girl would eat dirt on the street but would not tolerate a speck of dirt on the dining room table. Sometimes pica is practiced as an attention-getting device. Mechanical restraints are ineffective, but close observation of the child, strict supervision of what goes into his mouth, and appropriate training are effective. Green[8] maintains that perverted appetite does not necessarily indicate a defective mind, for the symptoms may occur in the mentally normal child.

Treatment of Elimination Disorders. Enuresis or involuntary micturition during the day or night abounds in the severe ament, but bowel and bladder control is achieved by the moderate ament at the same age as the normal child. Effective training is within the range of all aments, because intelligence is not the determining factor in vesicle control. Frary[7] found that enuresis is determined by a single recessive gene substitution. Heredity is usually the underlying basis, bed-wetting occurring in neurotic siblings and frequent voiding in neuropathic parents. The sensitive bladder persists throughout life in affected members of the family. Enuresis may be due to urinary tract defects or disorders. Congenital obstruction along the urethra is most common in boys, and ureterotrigonitis is most common in girls. The lesions are as individual as the child; hence the need for cystoscopic examination in the case resistant to therapy. Most cases of enuresis show no evidence of organic disease. Lesions of the spinal cord, responsible for incontinence in some enuretic aments,

should be distinguished from true enuresis. Motor abnormalities of the lumbosacral spine, demonstrable only radiologically, are never likely to account for the condition unless there is other evidence of nerve involvement.

Treatment depends on the underlying condition. Parents should assume an unemotional attitude and should refrain from rewards, punishments, and threats. The child should be cleared of the feeling of hopelessness about his difficulty because nervous tension aggravates vesicle irritability. Amberg[3] found that belladonna reduces bladder pressure. The ament should be given 5 drops of tincture of belladonna three times a day before meals, the dose gradually being increased according to tolerance and then continued for two months. Kugelmass[17] found that methyltestosterone, 10 to 20 mg. daily, improves the tonus of the bladder muscles. Amphetamine sulfate, 5 mg. on arising, eases anxiety in the hyperactive ament. Methantheline bromide (Banthine*), 25 mg. at bedtime, relieves urgency and frequency. Krasnogroski[13] found that 5 Gm. of salt added to the bedtime snack favors water retention during the night. A special apparatus has also been devised that rings a bell when a child starts to urinate and wets a pad on which he sleeps. Single or combined methods of treatment should accompany training and suggestion. The ament should be maintained on a relatively dry diet throughout the day. Sips of water, cracked ice, or a lemon drop quench thirst. Voiding intervals should be prolonged during the day, and the child should be awakened once or twice during the night to go to the toilet. A record of dry nights may call for appropriate rewards. Intractable cases may persist beyond puberty.

Encopresis. Persistence of fecal soiling beyond infancy in the absence of any organic lesion of the anus or rectum accompanies enuresis in the severe ament. The stools are soft and the evacuations frequent. The difficulty usually lies in improper toilet training, emotional maladjustment, parental dominance or rejection, or other parent-child difficulty. It is one of many ways the ament uses his body as a means of expressing his feelings. Fetal incontinence may be associated with constipation, the child retaining some of the stools for a while and passing them from time to time. Treatment involves a training program for bowel control. The procedure should be supplemented by measures corrective of the psychologic maladjustment of the child, while the stools are hardened by a bland binding diet.

Treatment of Sleep Disturbances. Restless sleep may be due to physical discomfort, intestinal digestion, excessive fatigue or stimulation, or emotional tension. More often it is a manifestation of resistiveness due to faulty training, parental rejection, fearfulness, masturbation, anxiety about separation for the night, or curiosity about adult activities. The ament refuses to go to bed, beckons someone to stay with him, wanders into the parents' bed, demands drinks of water, desires to go to the toilet, or complains of aches and pains. The ament should be put to bed regularly at the proper time while the mother remains occupied knitting or reading in the room, reassuring him calmly while he tosses, rolls his head rhythmically, grinds his teeth, makes jerking movements, sweats excessively, and cries out in his sleep.

In *sleepwalking*, the hysterical ament enacts a dream. The child seeks in fantasy

* The trade name of G. D. Searle & Co. for methantheline bromide is Banthine.

what he cannot achieve in reality. He has a definite objective in his walking. His eyes are open but he does not know what he is doing. He may stumble, avoid obstacles, yet be in danger. Precautions should be taken to prevent him from hurting himself. He is unaware that he has been out of bed, and when awakened during his somnambulism cannot describe the situation. Eliminating the sources of tension in his daily life subdues this familial neuropathic tendency.

Nightmares are fright reactions to dreams. The child wakes up in tachycardia and dyspnea, acts frightened, feels helpless, but recognizes his surroundings and remembers the dream the following morning. It usually occurs within an hour or two after going to bed and recurs again and again, heralding the same terrifying dream. *Night terrors* are hallucinations of imaginary figures in the room or dreams of injury from animals. The child sits up in bed or runs aimlessly about the room, the eyes wide with terror, clutching at his parents and screaming for help. He remains disoriented for 15 minutes in spite of all efforts to calm him and then goes back to sleep. This recurs nightly or at long intervals in the emotionally unstable ament, following some upsetting event, a harrowing television show, lurid bedtime stories, or intercurrent disease. At first *sleep talking* is fragmentary, with mumbled, unintelligible words reviewing the activities of the preceding day. Then the child becomes so disturbed that he cries and screams in terror.

Insomnia or wakefulness during the night requires reorientation of the training procedures before a sedative is offered. The drug of choice, diphenhydramine hydrochloride or phenobarbital, is given with the evening meal when there is difficulty in falling asleep or at bedtime when there is waking during the night. The late afternoon prelude to sleep should have a calming effect on the child. That time should be free from excitement, outdoor play, radio or television, or other stimulation. A warm bath before the evening meal followed by a pleasant story is reassuring.

Narcolepsy or excessive sleep may be a congenital tendency in boys or a defense mechanism to escape from duties. Recurrent diurnal attacks of irrepressible sleep may occur spontaneously or be induced by emotional disturbances. Sometimes they are associated with cataplexy with sudden loss of static muscular tonus. The ament's legs give way and he collapses on the ground unable to move his atonic muscles voluntarily, but there is no loss of consciousness. The attack simulates epilepsy, but the neurologic mechanism is the reverse of seizure. The lesion is in the diencephalon where brain centers control internal inhibition and voluntary muscular tonus. Narcolepsy may accompany organic disease, especially tumors in the floor of the third ventricle, epidemic encephalitis, diabetes mellitus, hypothyroidism, or cerebral injury.

Hypersomnia or persistent drowsiness apart from sedatives may be toxic or infective in the anemic ament. The body is devoid of stamina, the heart small, the blood vessels toneless. The cerebral vessels are badly filled in the erect posture, producing drowsiness. But the brain becomes hyperemic from dilatation of its toneless vessels in the recumbent position and keeps the ament awake during the night. Diurnal drowsiness and nocturnal wakefulness may be alleviated by ephedrine sulfate, 0.75 gr. once a day, or preferably amphetamine sulfate or dextro amphetamine sulfate, 0.5 gr. once a day.

Barbiturates have both sedative and hypnotic effects, but the ament tends to have a natural idiosyncrasy to them in the form of a hang-over, excitement, or pain. After the initial period of depression has passed, lassitude, vertigo, digestive and emotional disturbances, and phobias may be accentuated. In some aments, barbiturates produce excitement rather than depression. The short-acting barbiturate, such as hexobarbital sodium, thiopental sodium (Pentothal Sodium*), or secobarbital (Seconal†), is preferable to the long-acting aprobarbital (Alurate‡), diallyl barbituric acid (Dial§), probarbital (Ipral‖), butethal (Neonal¶), and phenobarbital. Hexobarbital sodium, 4 gr., secobarbital, 0.5 gr., or amobarbital (Amytal#), 1.5 gr., is preferable to pentobarbital (Nembutal**), 1.5 gr., or phenobarbital, 1.5 gr. A combination of dextro amphetamine sulfate, 5 mg., and amobarbital sodium, 32 mg., called Dexamyl†† provides a synergistic effect free from the dulling of the barbiturate and the excitation of the stimulant. When oral administration is not feasible, phenobarbital sodium may be dispersed in a few milliliters of warm tap water, introduced rectally with a size 14 Fr. catheter, a distance of six inches, offering 0.5 gr. for an infant, 1.5 gr. for a child, and 3 gr. for an adolescent. Subcutaneous or intramuscular injections of phenobarbital sodium may be given, 0.125 gr. in infancy and 0.5 gr. in later childhood.

Chloral hydrate is an effective hypnotic, with an effect lasting several hours. There is no risk of producing myocardial depression with ordinary therapeutic doses. It is a gastrointestinal irritant, hence best administered by rectal retention. The maximal hypnotic dose is 0.5 gr./lb. of body weight. The total dosage never exceeds 30 gr. at any age. An infant may be given about 2 gr., a young child 6 gr., an older child 12 gr., and an adolescent 25 gr., in 0.5 oz. of olive oil or water.

Bromide is the term used to refer to sodium bromide since the ammonium and potassium salts have no particular advantage. Sodium bromide is usually given in combination with chloral hydrate and in the same dosage. Bromide sedation develops slowly and dissipates slowly according to the level of circulating bromide ions. It may be given three times daily for sedation or combined with chloral hydrate at bedtime for a prolonged effect. Barbiturate and chloral hydrate produce transient sedation.

BIBLIOGRAPHY

1. Abood, L. G.: Personal communication.
2. Albert, K.; Hoch, P., and Warlsch, H.: J. Nerv. & Ment. Dis. *104*:263, 1946.
3. Ambero, S.: Am. J. Dis. Child. *41*:507, 1931.

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* The trade name of Abbott Laboratories for thiopental sodium is Pentothal Sodium.
† The trade name of Eli Lilly & Co. for secobarbital is Seconal.
‡ The trade name of Hoffmann-LaRoche, Inc., for aprobarbital is Alurate.
§ The trade name of Ciba Pharmaceutical Products, Inc., for diallyl barbituric acid is Dial.
‖ The trade name of E. R. Squibb & Sons, Inc., for probarbital is Ipral.
¶ The trade name of Abbott Laboratories for butethal is Neonal.
# The trade name of Eli Lilly & Co. for amobarbital is Amytal.
** The trade name of Abbott Laboratories for pentobarbital is Nembutal.
†† Manufactured by Smith, Kline & French Laboratories.

4. Axelrod, J.: Personal communication.
5. Cohen, R. A., and Girard, R. W.: J. Cell. & Comp. Physiol. *10*:223, 1937.
6. Erspamer, V.: Ricerca Scientifica *22*:1420, 1952.
7. Frary, L. G.: Am. J. Dis. Child. *49*:557, 1935.
8. Green, H. H.: Physiol. Rev. *5*:336, 1925.
9. Grenell, R. G.: Ann. New York Acad. Sc. (April) 1956.
10. Hamlin, K. E., et al: J. Am. Chem. Soc. *73*:5007, 1951.
11. Heim and Wallace: Quart. J. Exper. Psychol. *2*:19, 1950.
12. Himwich, H. E.: New York Acad. Sc. (April) 1956.
13. Krasnogoroski, N. I.: Monatschr. f. Kinderh. *57*:252, 1933.
14. Kugelmass, I. N.: Newer Nutrition in Pediatric Practice, Philadelphia, J. B. Lippincott Co., 1940.
15. Kugelmass, I. N.: Am. J. M. Sc. *208*:631, 1944.
16. Kugelmass, I. N.: Am. J. Digest. Dis. & Nutrition *11*:368 (Nov.) 1944.
17. Kugelmass, I. N.: J. Clin. Endocrinol. *6*:823, 1946.
18. Kugelmass, I. N.: Management of Mental Deficiency in Children, New York, Grune & Stratton, Inc., 1955.
19. McCulloch, T. L.: Am. J. Ment. Deficiency *55*:117 (July) 1950.
20. Marrazzi, A. S.: Personal communication.
21. Moustakas, C. E.: Children in Play Therapy, New York, McGraw-Hill Book Co., Inc., 1953.
22. Mullins, L. J.: Ann. New York Acad. Sc. *62*:247, 1955.
23. Nachmansohn, D., et al: J. Biol. Chem. *150*:485, 1943.
24. Price, J. C., et al: J. A. M. A. *122*:1153, 1943.
25. Quinn, K. V., and Durling, D.: Am. J. Ment. Deficiency *54*:321 (Jan.) 1950.
26. Rapport, M. M.: J. Biol. Chem. *180*:961, 1949.
27. Rosenberg, A. J : Proc. Third International Congress of Biochemistry, Brussels, 1955.
28. Ross, D. A., et al: Endocrinology *25*:75, 1939.
29. Rudolf, G. de M.: J. Ment. Sc. *96*:265, 272 (Jan.) 1950.
30. Seiger, H. W.: J. Pediat. *40*:738, 1952.
31. Shorvon, H. J., et al: Brit. M. J. *2*:951, 1949.
32. Sokoloff, L.: Personal communication.
33. Spies, T. D.: M. Clin. North America, p. 794 (May) 1945.
34. Thorne, F. C.: Am. J. Ment. Deficiency *52*:263, 1948.
35. Udenfriend, S.: Personal communication.
36. Woolley, D. W., and Shaw, E.: Proc. Nat. Acad. Sc. *40*:228, 1954.
37. Zimmerman, F. T., and Ross, S.: Arch. Neurol. & Psychiat. *51*:446, 1944.
38. Zimmerman, F. T.; Burgmeister, B. E., and Putnam, T. J.: Am. J. Psychiat. *105*:661, 1949.

Present-Day Concepts of Cerebral Palsy

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The story of those having cerebral palsy is one of children being hidden away in homes as "a curse on the family" or sent to mental institutions. There is no doubt that cerebral palsy has existed through the ages, but it was not until 1862 that William John Little, an English surgeon, published a monograph describing this condition. Little's description of the spastic, drooling, grimacing child with a "scissors gait" gave the erroneous impression that all children with cerebral palsy were of this type and were feeble-minded. The term "Little's disease" should not be used to describe all children with cerebral palsy, since we know that impaired intelligence does not necessarily accompany the motor disability and that spasticity is present in only one type of cerebral palsy.

Definition and Incidence. Cerebral palsy may be defined as a neuromuscular disability caused by lesions in the motor centers of the brain: before birth, at birth, or during infancy and childhood. The disturbances of motor function include spasticity, weakness, incoordination, athetosis, rigidity, and/or tremors. The brain damage may not only produce a neuromotor dysfunction, but frequently causes mental retardation, sensory disorders, convulsions, eye and ear disabilities, and behavior disorders as well. It is difficult to assess the number of children with cerebral palsy, but it is known that the incidence of this condition is exceeded only by that of poliomyelitis. It is estimated that throughout the United States there are approximately 550,000 persons with cerebral palsy, 200,000 of whom are under 21 years of age. Numerous surveys have indicated that approximately 1 infant in every 200 live births will be born with a brain injury, one every 53 minutes.

Etiology. The etiologic factors may be classified as follows: *Prenatal*—from the time of conception to the time of labor: (a) Hereditary—Tay-Sachs disease and tuberous sclerosis. (b) Congenital—anoxia, maternal infections, metabolic disease, and Rh factor. *Natal*—from the onset of labor to the birth of the child: (a) Anoxia—due to obstruction of the cord. (b) Asphyxia—as a result of mechanical respiratory infection. (c) Analgesics—affecting the respiratory center of the infant. (d) Trauma—injuring the brain during labor or by forceps delivery. (e) Sudden changes in pressure—as in cesarean section. (f) Prematurity. (g) Low vitamin K level. *Postnatal*—from the time of birth of the child: (a) Trauma—skull fractures or wounds. (b) Infections—meningitis or wounds. (c) Vascular—hemorrhage, thrombosis, and embolus. (d) Anoxia—carbon dioxide poisoning. (e) Neoplasms.

In an attempt to verify these observations reported in the literature, 100 children were selected at random from those under treatment in our clinic.[2] The attending physician, the obstetrician, and the hospital where the child was born each received a form to fill out pertaining to the pregnancy, the delivery, and the condition

of the child. After an analysis of these data and correlation of all factors, the following conclusions were reached: (1) Sex, the age of the mother, or being a first-born child were not predisposing factors. (2) Prenatal anoxia was considered an etiologic factor in 15 of our children with cerebral palsy. (3) Seven per cent of our cases were due to the Rh factor. (4) Two children had cerebral palsy due to infections in the mother.

Our impression from this study is that the case of cerebral palsy caused by a single etiologic factor is the exception, and that most cases are probably due to multiple factors.

EARLY SIGNS OF BRAIN DAMAGE

The growth and development of the normal infant usually follows definite motor, adaptive, language, and personal-social patterns. By observing the behavior patterns of any child the physician can match them against those of the normal child at the same age level and arrive at an estimate of the maturity level. Retardation in growth and development is usually observed if the brain has been damaged.

At 2 months of age the child shows some expression and awareness of his surroundings by smiles, frowns, and fixing of his eyes on moving objects. *Nystagmus, persistent head rolling, opisthotonos, and lack of facial expression* suggest brain damage.

At 4 months the tonic neck reflex should be absent and the head held in the midline. The child can raise his head from the supine position and turn it from side to side and hold his head erect when the body is supported in the sitting position. When the trunk is raised from the supine position, the head is flexed on the chest and there is no head lag. The child begins to reach and grasp with the hands. There is increased vocalization and laughter, and the attention span is sustained. The signs that indicate brain damage at this age level are *a head lag, Moro reflex, the hand closed over the thumb*, and *persistent strabismus*.

At 8 months the infant should be able to roll over from the supine to the prone position and to sit without support when placed in the sitting position. He reaches for and grasps objects and transfers them from one hand to the other. He vocalizes to playthings, turns toward sounds, recognizes his parents, and responds to his bottle and food. *A persistent tonic neck reflex, head lag, random automatic movements, adduction of legs when sitting, and kicking both feet in extension* suggest brain damage.

At 1 year of age the child begins walking without support, grasps and releases objects with his hands, and can pick up pellets by apposition of his thumb and index finger.

It is extremely difficult to diagnose cerebellar damage until the child begins to walk, as the signs of ataxia are difficult to elicit at such an early age.

METHODS OF CLASSIFICATION

Clinical Signs. The classification of types of cerebral palsy is based on the observable clinical signs.

The *spastic* type is characterized by signs of pyramidal tract involvement. There is a stretch reflex, the deep reflexes are increased in the affected parts, and the Babinski sign is present. To test for the stretch reflex, the muscle group is placed in the

contracted position and then suddenly moved in the opposite direction. If spasticity is present there will be a blocking or slowing up of the movement. Approximately 66 per cent of the cerebral palsy patients are of this type.

The child with *athetosis* presents slow, wormlike, involuntary, uncontrollable, unpredictable, and purposeless motions. About 19 per cent of the total number are of this type.

The *rigidity* type, which may be diagnosed by the resistance to slow passive motion, includes about 4 per cent of the cases of cerebral palsy. When the part is moved there is a continuous resistance in agonist and antagonist muscles, simulating the sensation of bending a lead pipe. In many cases the rigidity may vary from time to time, being present at one time and absent a few minutes later. The term "intermittent rigidity" is applied to this type. In many cases the rigidity is so great that no motion is present.

The chief characteristic of the *tremor* type is the presence of involuntary, uncontrollable motions that are reciprocal and regular in rhythm. Patients of the tremor type make up about 2 per cent of the total number of cerebral palsy patients.

The principal sign in the *ataxia* patient, estimated to be about 8 per cent of the total, is disturbance of balance and equilibrium. It is difficult to diagnose ataxia until the child starts to walk.

There are *mixed* types in which all these types may exist. Spasticity and ataxia usually appear as pure clinical types.

CLASSIFICATION ACCORDING TO EXTREMITIES INVOLVED

The terms generally used to describe this classification are as follows:

Paraplegia patients have their lower extremities involved and are practically always of the spastic type.

Hemiplegia patients have an upper and lower extremity involvement on the same side of the body.

Triplegia involves three extremities, usually both lower extremities and one arm, and the disability is usually of the spastic type.

Quadriplegia, tetraplegia, or diplegia patients have involvement of all four extremities. Almost all patients with athetosis have all four extremities involved.

PATHOLOGY

The literature usually states that when there is spasticity the lesion is in the cortex; that athetosis, rigidity, and tremors are due to pathology in the basal nuclei; and that ataxia is a sign of cerebellum damage.

Recent investigations from the study of the brains of cerebral palsy children emphasize the fact that frequently there is no correlation between clinical findings and the lesions found in the brain at autopsy.

SPECIAL EXAMINATIONS

As the brain is also the seat of intelligence, hearing, vision, and speech, it is

necessary to evaluate these functions before prescribing a program of treatment and prognosticating the future possibilities of the child and his progress.

Intelligence. The child with cerebral palsy is often considered mentally retarded because of his appearance and his inability to make normal responses. The testing of these children is made more difficult by the fact that many of them are unable to perform voluntary motions and/or speak, and there may be visual and hearing difficulties.

Studies of the intelligence of children being treated in cerebral palsy clinics show that from 60 to 70 per cent are mentally retarded.[3]

Speech. "It is estimated that 75 per cent of all children with cerebral palsy have speech defects and that from 50 to 75 per cent of these children can be benefited by speech training."[4]

The benefits that can be expected from a speech training program depend a great deal on the child's intelligence level, his visual and auditory loss, and the severity of the handicap.

Hearing. Children with cerebral palsy often have hearing disorders; these are found most frequently in the athetoid type. If there is any doubt, it is important to obtain some information as to the child's hearing ability before prescribing a program.

Vision. The rehabilitation of a cerebral palsy child depends to a great extent on his visual acuity. Guibor[5] states, and this has been our experience, that 50 per cent of patients with cerebral palsy have a strabismus as compared with 1 or 2 per cent of the general population.

Early treatment of these motor defects by means of atropine, glasses, and prism lenses is essential to conserve vision and improve coordination. Surgical treatment of strabismus in the athetoid is usually unsuccessful.

EVALUATION PROCEDURES

When a physician has demonstrated that the child has brain damage and the condition can be diagnosed as cerebral palsy, the following factors should be investigated: (1) Etiology—Congenital or acquired and possible cause. (2) Diagnosis—*The evidence of a neuromuscular disability must be obtained in order to diagnose cerebral palsy.* Mentally retarded children, because of their inability to sit, stand, walk, or talk at the normal age level, are often referred with a diagnosis of cerebral palsy. (3) Classification of type—Spastic, athetoid, rigidity, tremor, ataxia, or mixed. (4) Disabilities—The parts of the body involved; hemiplegia, paraplegia, etc. (5) Severity—Mild, moderate, or severe. (6) Consultations needed—If there is evidence of hearing or visual defects, orthopedic conditions needing evaluation, seizures, or congenital anomalies, consultations may be advisable before recommending treatment.

OBJECTIVES OF TREATMENT

The principal objectives of physical treatment are (1) to teach self-care activities, (2) to teach ambulation, (3) to obtain the maximum use of the hands, (4) to obtain adequate speech, and (5) to obtain the appearance of being normal.

These are the basic needs of any disabled person who expects to become independent of the help of others, to be able to profit from an education, and to obtain employment.

In order to evaluate the ability of the child to perform the activities of daily living he is given the A.D.L. Test. This test consists of activities in the following areas: Ward activities: 1. Bed activities (10), 2. Dressing activities (9), 3. Hygienic activities (11); Hand activities: 1. Preparatory activities (8), 2. Manipulatory skills (22), 3. Feeding activities (9), 4. Writing activities (5); Ambulatory activities: 1. Wheel chair activities (11), 2. Ambulation (7), 3. Climbing activities (15). Those activities the child cannot perform become part of the items in his daily program.*

No standard procedure has been developed that can prognosticate which child will benefit from treatment. Many physicians have based their selection of children to be admitted for treatment solely on the results of intelligence tests. A report from Duke University Cerebral Palsy Center states, ". . . there are several children in our hospital with reported I.Q.'s below 65 who, according to staff reports, are making excellent adjustment and exhibiting marked progress in treatment. However, there are other children of higher I.Q. who, despite comparable disabilities, appear to profit less readily by our treatment procedure."[6]

As yet, no one is able to predict what a well motivated child with even a severe disability and mental retardation can accomplish if given adequate treatment and if he has parents who are interested in helping their child.

GENERAL METHODS OF TREATMENT

Whatever method of treatment is used, the primary objectives are to make the child physically independent. The purpose of medical and surgical treatment has been to make it possible for the child to regain his health and strength so that he can perform the activities necessary for daily living and working.

Drugs. The drugs that have been recommended to control neuromuscular movements, such as spasticity and athetosis, have proved to be of little value.

There is no drug effective in all types of seizures, and it is necessary to experiment clinically with drugs in various combinations. All the drugs have some objections, either in the form of the side effects or in the tendency to aggravate certain types of seizures.[7]

Surgery. The purpose of surgery is to help the patient obtain better functional mobility in order that he may perform the physical activities essential for daily living. Operative procedures have no curative effect, and in the growing child, operation is often a useless procedure if therapy or braces are not prescribed. The greatest benefits are derived from surgery on the lower extremities of patients with the spastic type of cerebral palsy.

Exercises. Training the neuromuscular system to perform voluntary coordinated functional movements and maintaining the normal range of motion at the joints can

* This test, listing the items and methods of grading, can be obtained by writing to the author at 400 East 34th Street, New York City.

often be accomplished by specific forms of exercise. All programs of exercise should be given for the purpose of preparing the child to perform the functional movements essential to meet the demands of daily living. Training the child to abduct his arm at the shoulder has little functional value. If, however, the child can be taught to flex and extend the arm and grasp and release, he will be able to clean his teeth, wash his face, and feed himself.

Braces, Crutches, and Wheel Chairs.[8] The great majority of children will need braces, crutches, and a wheel chair in order to ambulate and care for their daily needs. After many years of training, some may be able to function adequately without any of these appliances, but the majority will need one or more of these aids for the rest of their lives. The physician responsible for the treatment of the child with cerebral palsy must be able to prescribe the proper braces, crutches, and wheel chairs for his patient at the time they are needed and, just as important, know when to reduce bracing, to change crutches and crutch gait, and to limit or eliminate the use of the wheel chair.

DISCUSSION

There are very few conditions that produce the many and varied disabilities, such as those found in the brain-damaged child. Few physicians have the time, interest, or facilities to treat these children adequately. Parents should not be told that nothing can be done for their child and that the best thing to do is to "put him in an institution." They will shop around and find some charlatan who will undertake some form of treatment. These children suffer from childhood diseases and need the care of a pediatrician; the parents need the supportive treatment of a physician. Practically every large city and many smaller cities have treatment centers for cerebral palsy to which these children can be referred for the specific therapies best suited to meet their needs.

CONCLUSIONS

In order to reduce the incidence of cerebral palsy, it will be necessary for the physician who is responsible for the care of the mother during the period of gestation and birth of her child to give more attention to those things that we now know may cause injury to the brain.

BIBLIOGRAPHY

1. Deaver, G. G.: Cerebral Palsy: Methods of Evaluation and Treatment, Monograph IX, New York, Institute of Physical Medicine and Rehabilitation, New York University–Bellevue Medical Center, 1955.
2. Greenspan, L., and Deaver, G. G.: The clinical approach to the etiology of cerebral palsy, Arch. Phys. Med. (Aug.) 1953.
3. Hohman, L.: Intelligence levels in cerebral palsy children, J. Phys. Med. 32:282–290, 1953.
4. Pusitz, M. E.: Speech correction in cerebral palsy, J. Speech Disorders *4*:207–218, 1913.
5. Guibor, G. P.: Eye defects seen in cerebral palsy, Crippled Child *30*:4–7, 1950.
6. Garmezy, N.: Some problems for psychological research in cerebral palsy, Am. J. Phys. Med. 32:6 (Dec.) 1953.
7. Perlstein, M. A.: Newer drugs in therapy of epilepsy. III, Medical Journal *99*:2 (Feb.) 1951.
8. Deaver, G. G., and Brittis, A. L.: Braces, Crutches, Wheelchairs, Rehabilitation, Monograph V, New York, Institute of Physical Medicine and Rehabilitation, New York University–Bellevue Medical Center, 1953.

Developmental Eye Disorders in Children

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With the development of better and more exact methods of diagnosis, ophthalmologists have found that age is no barrier to thorough examination of the eyes. For this reason, it is understandable that they not only suggest but also insist that each individual be examined at least once during infancy or early childhood. Many defects are not noted until after the child has entered school, at which time some defects have already become permanent.

There are, of course, various gross defects about which parents seek advice voluntarily. Of these, I shall mention first the congenital defects, which actually are fairly rare but which nevertheless deserve mention. Physicians everywhere are now aware of the part prenatal maternal infections play in the development of some of these congenital defects. The most commonly implicated, perhaps, is rubella, with which are associated cataract, buphthalmos, and pigmentary changes in the fundus. Other abnormalities that may be seen are microphthalmus, iris atrophy, nystagmus, and strabismus. Certainly the pediatrician should be aware of the possibility that these may exist in association with other abnormalities such as deaf-mutism, heart disease, and microcephaly and, therefore, should insist on a complete ophthalmologic examination. Similar ocular defects are also caused by other virus diseases such as mumps and morbilli.

In addition to these, one must bear in mind that ocular anomalies can and do occur in the presence of disturbed metabolism elsewhere in the body. Included in this group are such disorders as albinism, Niemann-Pick disease, Schüller-Christian disease, scleromalacia perforans, Gaucher's disease, gargoylism, as well as many other, rarer entities. Undoubtedly, there is a strong familial and hereditary history; children of a consanguineous marriage, particularly, should be examined carefully because incidence is highest in this group. Any sign of a defect such as nystagmus, strabismus, coloboma, lack of pigment, or lens changes merits a careful history and study. There are all stages of these anomalies to be found, from the forme fruste (incompletely developed type) to the fully developed form with all its ramifications.

Cataract. Another lesion with a strong hereditary tendency is congenital cataract. This is manifested as an opacity of the lens or its capsule, which may be present at birth or develop during infancy or adolescence. The only symptom accompanying the formation of an uncomplicated cataract is a gradual diminution of visual acuity. Complicated cataract may be seen following other diseases of the eye (iridocyclitis, choroiditis, glaucoma, or retinitis pigmentosa). As previously mentioned, it may also be seen with maternal rubella or certain metabolic disturbances. If there is marked interference with vision, the cataract will be noted early. In many cases, however, the opacities that are of the nonprogressive type do not interfere with vision and are discovered only by routine examination. The examination of infants or children with congenital cataract should include (1) observation of light per-

ception, (2) pupillary reactions, and (3) pupillary dilatation for ophthalmoscopic examination. Treatment depends on the amount of visual disturbance and consists of surgical removal. Other lens anomalies that may be seen are ectopia lentis (luxation), microphakia, aphakia, and lenticonus.

Glaucoma. Congenital glaucoma results from an interference with the filtration of fluid from the eyes owing to a defect at the angle of the anterior chamber and the canal of Schlemm. There is increased intraocular tension, which causes marked enlargement of the eyeball, known as hydrophthalmos or buphthalmos, since the cornea and the sclera yield because they are not yet firm enough to resist stretching. The cornea is enlarged, thin, bulging, and usually cloudy, and the sclera is thin and bluish, the uveal pigment showing through. Frequently, the affected child is not seen until hopeless enlargement of the eye has occurred. The disease is usually slowly progressive, and the treatment is quite disappointing. A few cases, treated early, may respond well, and therefore, the attempt at treatment is worth while.

Retrolental Hyperplasia. A condition that is, happily, becoming a thing of the past is retrolental hyperplasia. It deserves mention since it has been such a recent cause of blindness in premature children. It has been found that too much oxygen given to the premature child in the incubator will cause the formation of a fibrous membrane behind the lens which causes massive retinal detachment and for which treatment is hopeless. However, if the oxygen is regulated at a maximum of 40 volumes per cent, this will not occur.

Toxoplasmosis. A fairly recently recognized entity, generally occurring prenatally, is toxoplasmosis with associated chorioretinitis. The full triad of signs is: convulsions, chorioretinitis, and cerebral calcifications; however, the chorioretinitis may exist alone. Most characteristically, the macula is involved; there is a large atrophic area, outlined by pigment clumps. This is the healed stage. It may be accompanied by ocular maldevelopment or ocular malfunction such as microphthalmos, congenital cataract, optic atrophy, or papilledema. Diagnosis can be verified by a complement fixation test. Treatment is disappointing, and the prognosis for useful vision is poor.

Strabismus. The most common childhood disorder seen by the ophthalmologist is strabismus, in which parallelism of the two eyes is not maintained. This may be divergent, convergent, or vertical; it may appear shortly after birth or later. A childhood disease may bring out what has been a latent defect. Most often the strabismus is associated with an error of refraction, although there are cases of congenital paralysis of any one or all of the extraocular muscles. In all these cases, treatment should be instituted early, even as early as 18 months of age. The pediatrician who assures the parents that the child will outgrow his defect is being remiss, since without proper therapy, the deviating eye becomes progressively more amblyopic until it eventually becomes permanently so. Refraction is the first step in treatment; if there is only a slight refractive error, surgery is the next step. After the age of 4 years has been reached, orthoptic training should be attempted so as to establish fusion and stereopsis. Very little can be done to establish these after the age of 6 years.

I would like to emphasize here the fact that young children may be suffering from

errors of refraction even in the absence of strabismus. If there is lid inflammation, vertigo, headache, corneal disease, eye pain, or some sign of poor vision, this should be considered and ruled out. This is true particularly when the parents have some refractive error.

Infections. Inflammation of the fetal eye of virus origin and protozoan origin has already been discussed. Pyogenic infections may occur during the process of birth. The infections to be described now are those occurring at some time during childhood.

Although orbital cellulitis is a rarity now, it can happen and is manifested as great swelling of the lids, chemosis, exophthalmos, impairment of the motility of the eye, and pain. Complications include optic neuritis, thrombosis of the retinal veins and of the cavernous sinus, and occasionally panophthalmitis. One must investigate the accessory nasal sinuses for the source. Prognosis is good with the use of the appropriate antibiotics.

Many children are subject to an inflammation of the lids or blepharitis characterized by reddening and thickening and the formation of crusts and scales. Itching and soreness may accompany this, and rubbing of the lids is common with the added complication of infected glands. Treatment should be instituted early.

Occasionally, infants suffer from epiphora (overflow of tears). Before birth the nasolacrimal duct is closed by a mucous membrane that sometimes does not disappear after birth as it should. Massage of the region of the sac sometimes opens the passageway, but frequently the sac becomes infected. If the use of antibiotics does not correct the condition, the infant will eventually have to have probing of the duct under general anesthesia.

Various forms of conjunctivitis may also be seen; it may be bacterial, allergic, or traumatic in origin. In bacterial conjunctivitis, there is congestion of the palpebral conjunctiva with a mucoid or a mucopurulent discharge. Cultures will show the causative agent, and treatment consists of the proper chemotherapeutic or antibiotic preparations. Allergic conjunctivitis is a form that shows symptoms chiefly during the spring and summer months. Most patients can give an allergic history. Itching and lacrimation are prominent symptoms, and there are large flattened papillae seen on the upper palpebral conjunctiva (the well known cobblestone appearance). Hydrocortisone preparations have been of tremendous help in the relief of symptoms.

Infection of the cornea may occur as a result of an imbedded foreign body or of trauma. In this way, corneal ulcer may be seen. Formerly, a common involvement of the cornea was seen in the presence of tuberculosis or poor nutrition; this has since become a relatively rare condition. Ulcers form on the cornea and conjunctiva, greatly incapacitating the child. There is a favorable prognosis. Another disease that, fortunately, is being relegated to the past is interstitial keratitis, an infiltration of the deeper layers of the cornea due to congenital syphilis. There is a noticeable reduction of vision. Generally, treatment is of no avail, but it is worthy of trial.

One may also encounter a case of iridocyclitis or uveitis; this is not particularly common in this age group. Symptoms include severe pain, photophobia, lacrimation, and interference with vision. The etiology is usually indeterminable. Treatment with ACTH has been efficacious.

Neoplasms. Neoplasms are not particularly common in childhood. Those that

do occur include benign papillomas, angiomas, and dermoid cysts. If these interfere with function, they should be removed. Carcinoma and sarcoma are rare in children. In the orbit, one may encounter neurofibroma, aneurysm, meningocele, and osteoma. These are benign and are removed only because of interference with vision.

A relatively rare, but nonetheless important, malignant tumor occurring almost exclusively in infants and children is the retinoblastoma. Presumably, it starts in utero and follows a familial pattern. There are small, round, yellowish white nodules appearing on the inner surface of the retina with polypoid masses extending into the vitreous. Sometimes, the growth is bilateral. The tumor is usually first noted when it is large enough to produce a peculiar yellowish reflex of the pupil (cat's eye). Extension is by way of the optic nerve. There should be early enucleation of the involved eye with removal of the largest possible portion of the optic nerve. If the other eye is affected, radiation is occasionally helpful.

This paper is a brief discussion of the more common ailments, ophthalmologically speaking, that occur in childhood. It serves to re-emphasize the importance of early examination and therapy in both gross and latent conditions.

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Diagnostic Determinants of Orthodontic Disorders in Children

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The recognition of dental malocclusion in the permanent dentition is comparatively easy. The human dental formula is well known, and deviations in jaw and tooth relationship are easily recognized by the physician who makes this part of his routine examination of the child. Malocclusion of the teeth in the younger child whose teeth are a mixture of the deciduous and permanent dentitions is not always easily diagnosed, even by dentists in general practice. Such a diagnosis involves an exacting technique and it may require a series of examinations made at different time intervals.

The purpose here is to present briefly the approach of the orthodontist in determining the need for treatment and the various factors he must take into consideration when establishing a diagnosis and planning treatment. The foregoing should be of interest to the physician because orthodontists have found, as have others who treat children, that they cannot concern themselves solely with the malformation they are called upon to correct but must take into account the child as a whole. This approach necessitates interprofessional understanding and cooperation.

Knowledge of the medical as well as the dental history of the patient and assessment of his developmental growth are important in orthodontic diagnosis. Practitioners of orthodontics know that they are dealing with more than a local somatic problem of a biophysical nature, which merely requires the application of mechanical force to bring about desired changes in the dentofacial area. They realize that there are psychic involvements that are responsible for certain somatic changes as, for example, when the patient practices pressure habits, such as finger, lip, and tongue-sucking, that can affect dentofacial development. They know that growth whether normal or abnormal is always a factor in orthodontic therapy. They also take into account aberrations of physical growth and development of genetic, prenatal, postnatal, local, and systemic origin, which must be considered if successful terminal results to treatment are to be obtained.

CRITERIA FOR ESTABLISHING ORTHODONTIC DIAGNOSIS

The following diagnostic criteria are of especial importance in the practice of orthodontics: (1) medical and dental history of the family and patient, (2) height and weight, (3) skeletal proportions, (4) facial features and skin texture, (5) bone age determined by wrist roentgenograms, (6) endocrine balance, (7) dental age shown by casts and roentgenograms, (8) craniofacial contours, cephalometrics, and (9) classification according to a norm.

1. *Medical and dental history* inform us of the genetic endowment and postnatal

development and growth experience of the patient and guide us in our diagnosis and treatment planning.

2. *Height and weight* measurements are taken of the patient and compared to standards of height and weight according to sex and chronologic age. Wetzel's grid provides a method of using height and weight and chronologic age to determine advance in growth progress of the individual over a period of time. In this manner, height and weight provide a clue to physical growth and maturation.

3. *Skeletal proportions* are determined by the ratio between the upper and lower body segments divided at the symphysis pubis. At birth the ratio is 1:1.7 with the upper segment being longer. By age 10 the ratio is 1:1. Disturbance in skeletal proportion is found in certain endocrine disturbances.

4. *Facial Features.* The clinical appearance of the face is helpful in determining maturative growth. For example, the naso-orbital configuration in hypothyroidism (cretinism) is infantile while in the pituitary dwarf it is preadolescent. These patients look characteristically younger than their chronologic age. There are other facies useful in determining developmental growth in addition to the usual orthodontic criteria used to determine classification of facial abnormalities such as micro- or macrognathia and prognathism.

5. *Bone age* is an indication of maturative growth and physical development of the child and is determined by the time scale of appearance and progress of ossification as shown on standard roentgenograms of certain bones, such as the carpals of the wrist, the elbow, shoulder, hip, knee, and foot. Certain centers in the same person may indicate more or less advancement or retardation than others when examined at the same time. More than one center is usually used to establish bone age. Some centers of ossification are more active than others at a given chronologic age. For the orthodontist, the use of both hands and both wrists of the patient is considered adequate. When other symptoms are absent, confirmation with standards of maturative growth of wrist and hand roentgenograms is accepted to indicate the normal. In using the hands and wrists it should be remembered that, as a rule, no new centers of ossification appear in the wrist between the ages of 7 and 9 years. During these years more stress should be placed on the changes in the outlines of the epiphyses, phalanges, metacarpals, and carpals. A deviation of not more than one year in bone age from an accepted standard in the absence of other diagnostic criteria of a positive nature is usually regarded to be within the range of normal variation.

6. *Endocrine Balance.* Due consideration of endocrine correlation is indispensable in the diagnosis, prevention, interception, and treatment of dentofacial abnormalities. Elimination of endocrine disturbances can not only prevent but actually correct some dentofacial abnormalities. While skeletal development is primarily genetically determined, it can be modified by the endocrines. The hormones can influence not only growth, but also aging of the skeleton.

7. *Dental Age.* The stage of dental development is determined by the order of appearance, size, and amount of calcification of the tooth buds; deciduous and permanent tooth eruption; and closure of the apexes of the permanent teeth. The foregoing are compared to standard tables of normal dental growth and development. The progress of dental development is subject in large measure, but not as an in-

variable rule, to the same factors that influence skeletal development and general systemic maturation. Retardation of dental development and eruption and malalignment of the teeth and malocclusion may be due to some specific interference with the process of tooth development and eruption or with the growth of the bone surrounding the teeth. Delay in dental development is usually but not always proportional to that in endochondral, skeletal, and general systemic retardation.

8. *Craniofacial Contours*. Head circumference, cephalic index, and facial index indicate craniofacial growth progress. These are determined largely by anthropometric measurements and roentgenographic cephalometrics.

9. *Classification according to a norm* largely consists in the comparison of the dentition of the individual to the norms established by Angle and Simon.

LIMITATIONS OF ORTHODONTIC THERAPY

Today biophysicists believe that the human body, human physiology, in fact, life itself, can be made understandable through mathematical formulas. Norbert Wiener in his book on *Cybernetics* speaks of the "feed-back mechanism" as a principle by means of which someday, he feels, it may be possible to influence and control human growth, development, and function.

The "feed-back" in mechanics operates in closed functional systems, as, for example, in telephone communication. In human physiology, the act of mastication follows a "feed-back" pattern in that chewing can start as a voluntary act and then be continued by proprioceptive stimuli and so be performed involuntarily without involving the higher centers of the brain.

In 1949, I pointed out that the act of mastication is carried on by a closed functional system of muscles, bones, and teeth and that there is a "feed-back" mechanism in masticatory function in which some of the force exerted in mastication is fed back again to the bones and muscles.

The teeth thus form a part of a closed functional system, and their position cannot be changed permanently by orthodontic means or otherwise beyond an area within this system where they conform to trajectorial functional forces. This area may be termed the "area of tolerance." If teeth are moved beyond or outside of this area, they are then situated so that they do not conform with the trajectories of force generated in function. In these cases orthodontic treatment is not successful and is followed by relapse.

Unfortunately, where the "area of tolerance" is situated in a given patient, i.e., the limits within which the teeth may be successfully moved in the individual, is as yet unknown.

Attempts to learn these limits are to be found in research on muscle pressure and in cephalometrics. So far, however, we still have to depend largely on clinical experience. Anyone can move teeth. Where to move them and to have them stay in their new positions still remains the main problem and entails much practical, clinical experience.

If we ever arrive at the point when it becomes possible for us to influence the "feed-back mechanism" and so to change all of the components in the closed functional system of mastication, i.e., to change the attachments of the muscles and the

shape of the jaw bones as well as the position of the teeth, then it will become possible for us to establish and follow formulas for obtaining uniformly successful results in our orthodontic treatment.

Normality in occlusion of the teeth presents a wide range so that it is practically impossible to establish the exact prevalence of malocclusion in the child population. It is generally recognized that a large percentage of children show some form of malocclusion. Much of this malocclusion is preventable, especially when it does not involve systemic causes or deep-seated interferences with normal dentofacial growth.

While age of the child is one of the primary considerations in determining the need for orthodontic therapy, it should be recognized that age in years cannot be accepted as the sole basis for treatment. Dental development and skeletal maturation are of extreme importance in evaluating the need for and the time to start orthodontic treatment.

Measures to obviate incipient malocclusion may be undertaken with the deciduous, mixed, or permanent dentitions. However, extreme care should be exercised when introducing mechanical aids in an attempt to prevent the development of malocclusion during active growth.

During the transition period from the deciduous to the permanent dentition, certain physiologic adjustments must necessarily take place in the arrangement and occlusion of the teeth. The injudicious use of mechanical aids may interfere with the normal physiologic development, which of itself may frequently correct what seems to be a malocclusion.

WHAT THE PHYSICIAN CAN DO TO PREVENT MALOCCLUSION

1. Recognize normal occlusion in deciduous, mixed, and permanent dentitions.
2. Recognize early deviations from accepted standards in eruption, deciduous tooth exfoliation, permanent tooth development, and normal occlusion.
3. Recognize malocclusion as classified by Angle.
4. Recognize and eliminate harmful dentofacial habits.
5. Advise parents on the need for orthodontic care of children. Practitioners should recognize predisposing factors and incipient malocclusion and have a knowledge of growth and development of the dentition, especially in relation to eruption and occlusion.
6. When indicated, refer patients to medical specialists for diagnosis and treatment of systemic conditions with dentofacial correlations.

Surgical Management of the Undescended Testicle

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Cryptorchism is a common abnormality in the human being; fortunately, it is a condition that can be treated with a high degree of success, provided appropriate surgical measures are employed in its management.

In any discussion of the undescended testis, it is necessary to distinguish between "true" cryptorchism and a "retracted" testis. The latter is seen with great frequency in infants and young boys; there is a lively cremasteric reflex, which temporarily pulls the testis up into a high position. With increasing age, this reflex becomes much less active and the testis is permitted spontaneously to be lowered and to remain in the scrotum. When examining a child with this condition, a testis in the inguinal canal can be nudged by the doctor's fingers and can be pushed down into the scrotum. In true cryptorchism, the testis cannot be palpated, or if palpable, it cannot be pushed down into the scrotal sac. A retracted testis never requires treatment; a truly undescended testis will almost always need therapy at some appropriate age.

RATIONALE FOR THERAPY

The reasoning behind proposals for treatment of an undescended testis includes several considerations:

A testis that resides in the inguinal canal or rests against the pubic bone is much more subject to damage or trauma than is one that is made to lie in a yielding and protective scrotum.

There has been much discussion regarding the tendency of an undescended testis to undergo malignant degeneration, but it is extremely difficult to gather any statistics of value relevant to this point; certainly none have yet appeared that are convincing. The danger of malignant change appears to be far less than was expressed so often in the literature a decade or two ago. Hence, the surgical placement of a testis into the scrotum has little merit from the point of view of attempting to prevent neoplastic disease; indeed, there have been a few reports of malignant growths developing in testes some years after the performance of orchiopexies. There is, however, some advantage in bringing a testis out of the abdomen or down from the canal into the scrotum where any subsequent new growth (if it should appear) can be quickly and more readily detected.

The endocrine output of a testis is apparently about the same whether the gonad is undescended or lies in a normal position. Hence, orchiopexy should not be recommended on the basis of maintaining or improving hormone production.

It is well known that a testis that resides in the canal, and particularly one that is

in the abdomen, has a greatly reduced formation of spermatozoa. If the patient has unilateral nondescent of a testis, probably little will be gained by orchiopexy, since the contralateral gonad will provide sufficient potency and fertility. In contrast, in a patient having bilateral cryptorchism, fertility is a prime consideration. Only a very small percentage of patients reaching adult life with untreated bilateral cryptorchism have been shown to be fertile. Therefore, the strongest indication for orchiopexy relates to those boys with bilateral maldescent of the testes who will almost certainly become sterile in adult life if one or both testes are not brought down into the scrotum by surgical means.

Finally, there are cosmetic and psychologic considerations, which indeed are well worth emphasizing. While a boy seldom expresses regret if a testis is not present in the scrotum, an adult is very likely to believe he is deficient if the genitals are not normal. To avoid psychologic reactions or feelings of insufficiency during subsequent years, it is best, whenever possible, to bring a testis down into the scrotum. Indeed, this is probably the outstanding reason for treating an undescended testis (except in those patients with bilateral involvement, where fertility takes first consideration).

OPTIMUM AGE FOR THERAPY

There is universal agreement that a testis which resides in a position outside of the scrotum after puberty will have great deterioration of its spermatogenic power, and that there will be little or no return of spermatogenesis if such a testis is placed in the scrotum thereafter. These facts have led to the widespread acceptance of the idea that treatment of an undescended testis should not be delayed beyond the age of 11 or 12 years.

Since 1950, several groups of investigators have made histologic comparisons between testes that are undescended and those that are residing normally in the scrotum, making observations on infants and boys of all age groups. There is reasonably close agreement among most of these authors regarding the histologic sequences that can be found: Except for the occasional testis that is obviously grossly deformed or atrophic, it can be said in general that until the age of 5 years there are only minor differences between the undescended organ and the normally descended one. From 5 years onward to puberty, there is a definite lag of enlargement of tubules in the undescended testicle when compared to the prominent increase in diameter of tubules of a normally placed testis. These findings have led some to suggest that it is imperative to operate before the age of 5 years on all boys with undescended testes. This reasoning is somewhat fallacious, because it is quite conceivable that a testis that is transplanted to the scrotum after the fifth year (but before puberty) can catch up in its development and can become a very satisfactory gonad. Furthermore, no one has presented any subsequent studies to prove that operation in the earlier years (before 5 or 6) is followed by results any better (from the standpoint of fertility) than those that have been obtained in patients operated on during the prepubertal years. Since it is technically much easier and safer to perform an orchiopexy on larger individuals, there is considerable justification for continuing the practice of advising therapy somewhere between the ninth and eleventh years. We are strengthened in this view by the fact that our studies of men

who had had operation between 10 and 12 years of age have shown much higher postoperative fertility rates than any other author has ever recorded.

Our policy of practice can be stated as follows: If an accompanying hernia is troublesome, operation can be performed at any time in infancy or early childhood, concurrently repairing the hernia and performing an orchiopexy, even though the young age of the child might not give the optimum size of individual for accomplishing the testicular mobilization. In the vast majority of cases, accompanying hernias cause relatively little concern and therefore the combined operative repair can be deferred until the optimum age, which is somewhere between 9 and 11 years.

HORMONE THERAPY

Hormone therapy for undescended testis is rapidly falling into disuse. It is quite probable that most of the so-called "successful" results following this mode of treatment have been in boys who had "retracted" testes, in whom the testes would have come down spontaneously in subsequent years when the individuals began to produce their own gonadotrophic hormones in sufficient quantity. In a truly undescended testis, there is a mechanical anchorage of the organ or else a blockage in its downward pathway, which cannot be overcome by the administration of gonadotrophic substances. Except for the very rare individual who has a Fröhlich type of development as a part of the over-all picture, we have completely abandoned hormone therapy for the past two decades.

METHODS FOR SURGICAL CORRECTION

Since undescended testes are accompanied in about 90 per cent of instances by an indirect inguinal hernia, the surgical undertaking is a double procedure for simultaneous handling of these two conditions.

The operation that is most widely used in this country today for treatment of an undescended testis is that popularized by Torek, or some slight modification of this technique. As it is generally carried out, there is very little dissection and freeing of the cord structures, following which the testis (or its tunica or gubernaculum) is sutured to the fascia of the thigh, this anchorage being maintained for some months, after which the testis is detached from the thigh and allowed to reside in the scrotum. There is very convincing evidence that this procedure is directly responsible for the large number of failures that various surgeons both here and abroad have reported after orchiopexy. The rigid and unyielding anchorage to the thigh is very likely to damage the delicate blood supply of the testis, thus leading to atrophy and to loss of fertility. In spite of the fact that the Torek operation is extensively employed, I feel it should be completely abandoned.

A suitable technique for performing orchiopexy requires certain fundamental and important steps and considerations, conformity to which gives an operative endeavor productive of highly satisfactory results. These principles can be summarized briefly as follows: (1) A wide operative approach throughout the length of and, indeed, extending beyond the inguinal canal, thus permitting a liberal retroperitoneal dissection and mobilization of the vas to the base of the bladder and a

freeing of the internal spermatic vessels well up toward the lower pole of the kidney. (2) The freeing of the testis from all surrounding attachments and a complete division of all cremasteric muscle fibers to give maximum mobility to the gonad. (3) The forcible digital stretching of the scrotal sac on this side, intentionally disrupting the dartos sheath and the contracted structures of the scrotal wall. (4) Threading of the lower pole of the testis with a traction suture, which is then led out through the lower pole of the scrotum, permitting pulling of the testis down into a scrotal position. (5) Giving the shortest pathway for the spermatic vessels to traverse, thereby allowing the testis to drop to its lowest possible position. To accomplish this, the internal inguinal ring is constructed just above the pubic bone, bringing together the various layers of the abdominal wall lateral and superior to this. (6) Attachment of the traction suture to a rubber band which is then stretched and anchored (by adhesive tape) to the thigh for about six days. This provides a *yielding* type of pull, which always gives some tension on the testis, but at no time does it reach a destructive level, regardless of the position or any movement of the leg.

This latter type of operation, if carefully performed, is a very satisfying one. It has clearly defined anatomic steps, and the dissection permits placement of a testis into the scrotum in well over 90 per cent of cases. By such careful manipulations, it is possible to feel assured that the blood supply of the gonad will not be impaired at operation or during the patient's convalescence.

RESULTS OF TREATMENT

Over a period of many years, nearly 1300 operations have been performed for undescended testis at The Children's Hospital of Boston. In about 3 per cent of these patients, no testis could be found in the canal or during the extensive retroperitoneal dissection. In a small percentage of cases, the testis was found to be small and underdeveloped, and it always remained so thereafter. In a few patients, the testis appeared to be normal at operation but subsequently became atrophied because the blood supply had been damaged by the surgical manipulations. In occasional cases, the cord was so short that the testicle could not be brought down into the scrotum in a single procedure, thus requiring a two stage mobilization, which we have always found to be effective and successful in placing such a testis well down into the scrotum. In an occasional patient, a testis has not stayed permanently in the scrotum, but has retracted up to the superior part of the sac, or even a little higher. All of these various disappointing results have totaled about 6 per cent in our series.

As judged by postoperative observations on the size, contour, consistency, sensitivity, and position of a testi., we have found that a little more than 90 per cent of all patients operated upon can be given a good result. It is difficult and almost impossible to estimate what power the unilateral surgically treated testis possesses for producing spermatozoa, because the contralateral normal gonad simultaneously carries on this function. However, a study of 38 men examined 10 or more years after surgery for bilateral cryptorchism (operations having been performed between the tenth and twelfth years of age) showed high fertility in 80 per cent. These observations have shown conclusively that not only can good cosmetic results be obtained by operation but that formation of spermatozoa is likewise made satis-

factory in the vast majority of instances. It is important to bear in mind that these excellent results have been obtained not by a Torek procedure, but by the use of the surgical principles enumerated above.

SUMMARY AND CONCLUSIONS

Contrary to the opinions expressed in so many articles in the medical and surgical literature, we feel it can be stated without hesitation that orchiopexy is an operation of outstanding merit and is one that can be followed by exceedingly good results, as judged postoperatively by the physical characteristics of the testis, by the position of the testis, and by the fertility of the individual in subsequent adult life.

Operations of the Torek type should be completely discarded in favor of procedures that focus on a wide and extensive liberation of the vas and internal spermatic vessels, a division of all the cremasteric muscle fibers, a forcible manual stretching of the scrotum, and establishment of an elastic form of traction for about a week after operation. Recognition of these principles and the use of care and delicacy in performing the various steps of the surgical undertaking provide a form of therapy that is outstandingly successful.

IN THE JUNE ISSUE OF

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Management of Mongolism in Childhood

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Mongolism is a syndrome characterized by certain rather constant anatomic peculiarities and by mental deficiency. Variations in the anatomy of the face and eyes give a Mongoloid appearance, hence the name.

The incidence of Mongolism in this country is approximately 1 in every 500 to 700 births. It occurs with greatest frequency in the Caucasian race, considerably less frequently in Negroes, and rarely in true Mongolians. While the over-all incidence is not great, the importance of Mongolism lies in the fact that it constitutes the largest single group of mentally retarded individuals requiring custodial care, and in the fact that it is by far the largest group in which a diagnosis of mental retardation can be made at birth. Every physician with an active obstetric or pediatric practice is almost certain, therefore, to be confronted sooner or later with the problem of dealing with such an infant and its unfortunate parents.

The distinguishing characteristics of Mongolism as seen in the newborn infant are, as a rule, quite obvious. This is particularly true of the facial appearance. The eyes have an upward and outward slant or appear to have because this feature is often accentuated by the presence of an epicanthal fold. The palpebral fissure or eye slit is short and often narrow, the nasal bridge is low, and the cheekbones high. The head is brachycephalic, and usually its circumference is slightly below the average. The occiput is usually flat and frequently the ears are low-set and misshapen or crumpled. The mouth looks small, the lips are thin, the tongue tends to protrude, and a highly arched palate is usually seen on inspection. At the nape, there is often an excess of loose skin and subcutaneous tissue. Muscular hypotonicity is observed in nearly all cases and also a poorly performed, floppy, and weak Moro reflex. The hands tend to be broad and thick, the thumbs stubby and flat, and the little fingers short and incurving. The pattern of palmar skin markings as revealed in palm prints is said to be distinctive and of diagnostic significance. The feet too are often broad and stubby, and in many instances the great toe is rather widely separated from the other toes, giving a thumblike appearance often exaggerated by the presence of a deep longitudinal plantar crease. In both males and females, the external genitals tend to be small. There is usually no breast engorgement, even in those born at term. A congenital heart defect is present in a relatively high percentage of these infants; usually it is a septal defect in the lower part of the interauricular septum. All of these peculiarities will seldom be simultaneously present in a single case.

The exact etiology of Mongolism is not known. That it results from defective development of the embryo is obvious. The fact that various anatomic abnormalities, particularly those of the brain, facial bones, and other skeletal structures, present themselves with such constancy as to produce a readily recognizable syndrome indicates that some factor, factors, or combination of factors interfered with normal embryonic development at a quite precise gestational age, synchronous with an active

stage of development of these particular structures. Studies indicate this to be very near the eighth week. The factor or factors responsible are not, at present, clearly understood. A direct correlation with maternal age has been statistically established. The incidence of birth of a Mongoloid infant to mothers between 18 and 30 years is relatively constant, but from a maternal age of 30 years on, the incidence increases regularly and significantly. Why maternal age is so related is not known. The age of the father is not a factor.

Studies of environmental factors have not yet revealed anything conclusive but the studies are continuing. The established causal relationship of rubella to congenital malformations, plus the demonstrated effect of environmental changes in pregnant experimental animals on the emergence of congenital malformations in the offspring, give stimulus to these studies. It is known that certain quite constant malformations appear in the human infant if the mother has rubella at a rather precise stage of early pregnancy. Likewise, in experiments with animals, the insult to intrauterine environment produced by low oxygen pressure or cortisone administration causes malformations in the offspring only when these insults occur at a precise stage early in gestation. Genetic factors also need further study. There is as yet, however, no specific evidence that conclusively indicts them. An interaction of genetic and environmental factors may be the answer.

The clinical course of Mongolism is of interest from several standpoints. One is the uniform pattern of the child's development, which makes his ultimate status predictable to a high degree of certainty. To see 20 to 30 Mongoloid children of about the same age together in a group, as I have in an institution, is a startling experience. Their looks and mannerisms are so much alike, they can hardly be told apart. And too, their ultimate developmental ceiling varies little. Many reach a developmental status comparable in many respects to a normal 6 year old; seldom, however, as high or higher than that of a 7 year old. The course is of interest also in the great variation in rate of development in the first year or two of life. Some progress at a rate so nearly that of a normal child as to make one momentarily question the diagnosis, while in others, developmental progress is extremely slow. Nearly all will ultimately learn to walk and to talk after a fashion. Few learn to read. They are great mimickers and learn to perform routine tasks usually very accurately and well. In their early years, they are happy and amenable members of the family group.

Because of a peculiar susceptibility to infection, many in the past died at an early age, but early death from infection is today much less common. The congenital heart defects found in quite a large number are now the chief cause of physical debility and death.

Diagnosis is made from the presence of certain stigmata of the syndrome mentioned above. By no means will all of them be present in each case. Those most commonly seen in my experience in order of diagnostic importance and constancy are: the Mongoloid appearance of the face, brachycephaly, flat occiput, poor muscle tone, "floppy" Moro reflex, thumblike appearance of the great toe, excess of soft tissue at the nape, small genitals, and absence of breast engorgement. All of this refers to the newborn period. This is an important consideration because the diagnosis can and should be made at this time in at least 90 per cent of the cases.

TREATMENT

There is no medical treatment of proved value. Glutamic acid, thyroid extract, and extract from the pituitary of fresh whole calves have been used, but without conclusive evidence of benefit.

MANAGEMENT

The diagnosis is made, and now the physician must decide how to handle this unhappy situation. When should he tell the parents? What should he tell them? What advice should he give? It is a heavy responsibility, a delicate situation requiring wisdom, courage, and tact. But it is his duty, and I know of none more difficult to perform. Physicians handle this situation in a variety of ways. It is my purpose in what follows to express an opinion regarding the answers to these questions. These opinions are my own, based on experience with a large number of Mongoloid children and their families during many years of active pediatric practice.

(1) *When should parents be told* that their infant is Mongoloid? As soon as the physician is quite sure of the diagnosis. There are three reasons for this: First, it is the parents' right to know what the physician knows about their baby. Second, it is unfair for the physician to be obliged to carry in secrecy and alone a burden that rightfully should be shared by the parents. I know of no task more difficult to perform nor one that requires more tact, but it should not be delayed or evaded. And third, early knowledge of the problem they face is of the greatest importance to the parents in their acceptance of, and adjustment to, their responsibilities, and in their success in working out an intelligent solution to their problem.

(2) *What should parents be told and how?* The facts should be told frankly, truthfully, and in full. Nothing good comes from shielding parents by withholding important information about their baby's condition and prognosis. The telling must be done with gentleness and sympathetic understanding, and the physician should be prepared to answer their questions patiently, thoughtfully, and as truthfully as his knowledge and experience permit. The initial telling need not, and probably should not, be an exhaustive discussion of all facets of the problem; in fact, it cannot be. The parents will be unprepared to bring up many questions they will later wish answers to; so the physician must expect and be prepared for repeated conferences, not only with the parents, but also with relatives.

(3) *What advice should the physician give?* He should be prepared to offer suggestions and general advice, but it is my firm conviction that he should never insist on any particular method of procedure. It is, after all, their problem and they alone can solve it. After they have been presented with the facts, they must have time to think it through in the quiet of their own home environment after the initial emotional shock has subsided and they can appraise it more objectively. The physician can tell them what other parents have done under similar circumstances, but the final decision must be their own. Their future happiness will depend on the peace of mind and soul that comes from the knowledge of having done what they believed right for them, their child, and their family.

The right solution for one family is not necessarily the right one for another. There are differences in cultural, educational, and religious backgrounds, differences

in family group situations, in temperamental and emotional stability of parents, and many other variables that have a bearing on the decision in individual cases. No matter how wise the physician, the priest, pastor, rabbi, or other friend who offers advice may be, he does not have infinite wisdom. Only the parents can make the decision that is best for them.

All of this is not meant to imply that the physician's duty consists only in stating the facts and offering initial advice. The parents have a right to expect from him continuing supervision of the child and moral support and guidance for themselves. This necessitates knowledge of such public or private facilities and agencies of the community as may be useful and necessary. The physician is in a strategic position to perform these functions, and the manner in which he assumes these responsibilities may well have far-reaching consequences in the welfare of the child and his family.

The physician needs to have an appreciation of the impact of this unfortunate situation upon the family in order to be of greatest help to them. In their adjustment, their first step is the acceptance of the fact that the infant is Mongoloid. They need assurance that there is no disgrace in this; it can happen in any family through no fault of the parents. Their second step is acceptance of the responsibility for the child and his welfare. Some have advocated the immediate placement of a Mongoloid infant in a foster home without even taking him home from the hospital after his birth. This, in my opinion, cannot be justified on any grounds, and I have never known it to be a satisfactory procedure. It is rejection of responsibility for the child simply because it happens to be born with a brain not capable of developing to a normal level of mental function. The third and final step is the decision by the parents on the course of procedure they feel is best for them to follow. There are various ways in which parents can successfully and adequately manage their problems. There can be no just criticism of any of them provided the parents have accepted their responsibility and chosen the course they believe best for them.

There are certain fairly well accepted facts regarding the natural clinical course of the Mongoloid child that can be used helpfully in giving advice to parents. These are that: (1) they are in their early years happy, playful, and easily manageable; (2) they have definite developmental potentialities that in a favorable environment will give them the ability to care for themselves and perform useful services under supervision, and the best environment for such development in their early years is usually the home; (3) the presence of a Mongoloid child in the home need not necessarily adversely affect the happiness and welfare of the parents or of other children in the family; and (4) the time will come when the home may no longer be advantageous to the child's developmental progress and he will be better off in an institution for mentally retarded children.

SUMMARY

Certain information about Mongolism has been presented in regard to its early recognition and management. The potentially strategic role of the physician in this medical and social problem has been emphasized in the belief that when this role is recognized and intelligently performed, the welfare of Mongoloid children and their families will be significantly benefited.

The Figure-Ground Syndrome in the Brain-Injured Child

Heinz Werner, Ph.D., and Alastair Weir, Ph.D.†*

One of the most fundamental and primitive activities of the organism is the formation of figure-ground relationships, a process first analyzed by Rubin[3] in the field of visual perception. Extending this relationship beyond perception, Goldstein[1] saw figure-ground configuration as the basic principle of neuropsychologic organization. In his view, a decrease in the organism's efficiency will produce a leveling of figure and ground processes, normally sharply contrasted with one another. In the following, evidence will be presented, mainly from the work of Werner, Strauss, and their collaborators, showing how such disturbances, which we shall call the figure-ground syndrome, affect the organism's functioning in different types of activity.

In these investigations, children were drawn from three main categories: (1) healthy children of normal intelligence; (2) mentally retarded children whose deficiency—at the borderline and moron level—was of the so-called endogenous, familial, or hereditary type; and (3) mentally retarded children—again at the borderline and moron level—who gave indications of a brain lesion acquired at birth or early infancy. The three groups of children were closely matched in regard to mental age.

We shall discuss figure-background impairment in relation to three areas of functioning: perception, memorization, and conceptual thinking.

PERCEPTION

In a study using the Rorschach test[5] it was found that brain-injured children differed significantly from mentally retarded children of the familial type in regard to the percentage of so-called "white space" (S) responses. S-responses are those in which the white areas of the Rorschach card, normally seen as background, are used figurally in forming a perception. This type of response, indicating a deviation from the normal figure-ground configuration, was found more than twice as often in the brain-injured group as in the endogenous.

Another investigation[11] used a series of "figure-background pictures," consisting of black and white drawings of objects, such as a hat, a teacup, a milk bottle, a knife; each of these figures was embedded in a background composed of regular patterns, such as jagged lines, little crosses (fig. 1). If the children were allowed to examine each picture at length, all of them recognized the figures (as well as their backgrounds) within a few seconds. If, however, the pictures were presented for one-fifth second, the brain-injured children had much more difficulty than the others

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FIG. 1. Tachistoscopic test card.

in recognizing or even perceiving the figures. While most of the children in the normal and endogenous groups perceived the figure, the brain-injured children frequently described the background, failing to perceive the foreground forms. These results were largely confirmed in a rigorously controlled study[2] of three sets of twins, where one member of each set was normal, the other brain-injured. Throughout, the brain-injured children were much more susceptible to background stimuli and to background interference than were either the endogenous children or the normal children.

While we are still considering figure-ground impairment in the visual field, two experiments employing two forms of the Werner-Strauss Marble-Board Test are of interest. In the first,[6, 10] the board used contained 10 rows of 10 holes each, in which marbles could be placed. The experimenter would construct a mosaic pattern that the child was asked to copy on another board. In this situation, the construction of the exogenous children was considerably interfered with by the horizontal-vertical arrangement of the holes in the board; in contradistinction to the endogenous children they had, for instance, great difficulty with diagonal-line figures (fig. 2). In

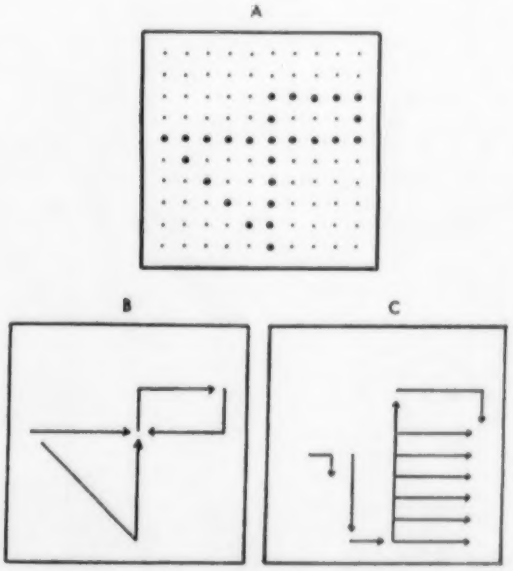

FIG. 2. Werner-Strauss Marble Board Test I, pattern 1. A: Model. B: Copy by endogenous child. C: Copy by brain-injured child.

the second study,[11] the boards contained many small triangular patterns of holes that formed a definitely structured background. Here, in order to copy the experimenter's marble pattern, the child had to work against the strong influence of the background patterning. The great majority of the brain-injured children's responses showed interference by the background pattern, while few of the endogenous group's responses were of this kind. The children were then asked to draw the experimenter's original design, which was still before them; these drawings again gave evidence of a much higher degree of background interference in exogenous compared with endogenous children (fig. 3).

That such figure-ground disturbance was not restricted to the visual sense was demonstrated in a study[11] in which the tactual-motor field was investigated. Here the children were required to draw three simple geometric figures that they had not been allowed to see but only to explore tactually. The figures were presented on two sets of boards. In the first set the background was composed of rows of flat enameled thumbtacks; the figure was formed by semispherical rubber tacks rising 5 mm. above the structured background. In the second set the background was smooth and flat, and the figure was a raised wooden solid. With the first set, almost all children of the endogenous group made straight-line drawings of the figure; in only a few cases were the background circles represented. On the other hand, most brain-injured subjects made drawings that indicated background interference (fig. 4). On the second set, where there was no structured background to interfere, none of the children had any difficulty in producing a more or less correct straight-line drawing.

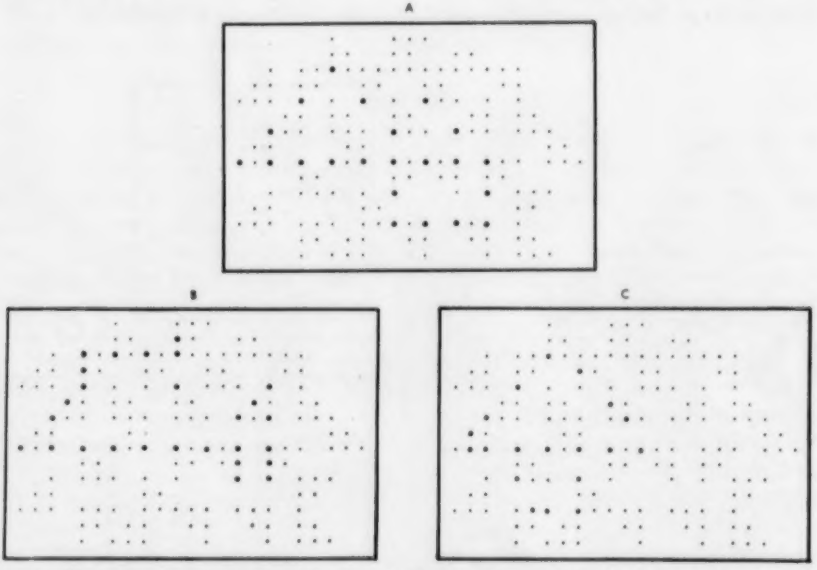

FIG. 3. Werner-Strauss Marble Board Test II. A: Model. B: Copy by brain-injured child. C: Copy by endogenous child.

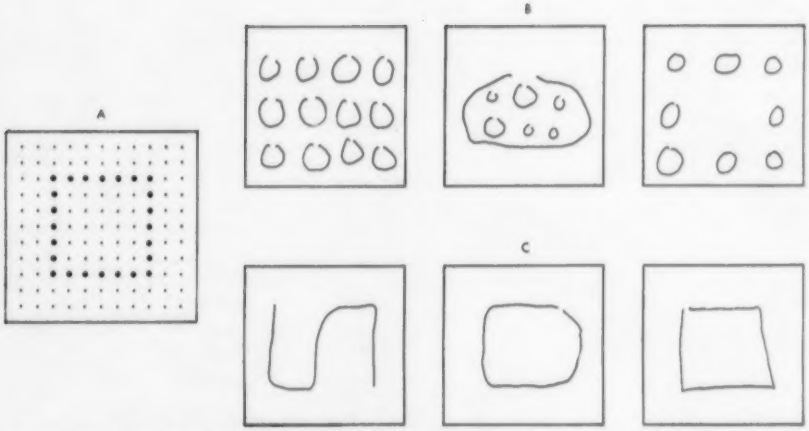

FIG. 4. Tactual-motor test pattern. A: Model. B: Copies by brain-injured children. C: Copies by endogenous children.

A similar breakdown of figural structure in exogenous children has also been observed in the reproduction of auditory patterns.[9]

MEMORY

Two experiments[7] may be cited that provide us with information on figure-ground disturbance within the area of memorization. In the first, a series of dot patterns was presented tachistoscopically and the child was asked to reproduce each immediately after it had been shown. First, three patterns similar to one another in general shape were shown three times each, after which four further patterns were shown once each. These were neither similar to one another nor to the previous group. The most interesting type of response here was that in which the child, on being shown one of the nonsimilar figures, reproduced instead one of the previously seen similar figures. This response can be held to represent an interference by the structure of earlier "background" memories, resulting in a failure to retain the organization of the figure just seen. This response occurred significantly often in the brain-injured children, not at all in the endogenous.

The same general method was then applied to the memorization of word lists. A list of four words was repeated and then reproduced four times, after which a different six word list was presented and reproduced once. Again the percentage of "importations" from the earlier into the later list was significantly greater in the exogenous than the endogenous children, suggesting that in the field of memory also, the brain-injured child is the more susceptible to background interference.

CONCEPTUAL THOUGHT

For the purpose of analyzing conceptual impairment in brain-injured children, Werner and Strauss constructed the following "Picture-Object" test.[4] Here, the

child was shown two upright pictures, one of a boy surrounded by waves and about to drown, the other of a building on fire at night, with firemen attempting to save the house. The child was then given a large number of miscellaneous toy objects and asked to place each one in front of the picture into which it would fit best. The results from this experiment showed that the thinking behavior of the brain-injured children was modified by their forced responsiveness to extraneous stimuli in the form of nonpertinent characteristics of the choice objects. Instead of "sticking to the theme" and selecting from the general group of objects only those that were appropriate to the task, they often were attracted by irrelevant objects, grouping together many of these into rather arbitrary combinations that had little or no connection with the picture. As an example, one brain-injured child grouped the teacup, matches, cigarette, and chair before the "fire" picture, saying, "The chair is for the fire chief to sit on; matches, teacup, cigarette, belong to the fire chief." Thus, here again we may characterize the impairment of the brain-injured children as an inability to prevent background stimuli from coming into the foreground.

Another test of conceptual processes involved the composition of a story by means of pictures.[8] The story was divided into three sections concerned with children (a) getting up in the morning, (b) on their way to school, and (c) in the schoolroom. The child had before him three empty stage settings corresponding to the three sections of the story; in front of each stage there were 50 upright pictures of single objects, persons, and scenes. From these he had to select and to place into each stage the pictures that, in his view, told the story best. The back of each stage consisted of a photo-montage of irregularly placed pictures of objects and scenes, many of which were quite unrelated to the task. In order to construct his story coherently, the child had to resist these irrelevant stimuli. In particular, certain of the single pictures (the "critical" pictures) were definitely related to the background pictures, but not to the story. The more often the child chose one of these critical pictures, the more (we may conclude) he had been influenced by the background pictures. In fact, the normals never chose the critical cards; the endogenous virtually never; the exogenous, as well as a group of spastic children, relatively often. In the absence of the background pictures, the critical cards were hardly ever chosen by either the brain-injured or spastic children, showing that their previous choices of these cards could only have been due to their own greater sensitivity to background interference.

CONCLUSIONS

The above series of studies leads clearly to the conclusion that brain-injured children are much more liable to interference from background stimuli than are endogenous or normal children. In contrast to the performance of endogenous defectives as well as that of normals of the same mental age, brain-injured children show a partial breakdown or leveling of the normally sharp distinction between figure and ground processes.

By referring to the disturbance as "figure-ground" syndrome we do not imply, however, that one is dealing here with an impairment of a unitary function. The

figure-background organization is rather conceived here as a psychobiologically fundamental performance of the organism that may be impaired because of a number of disturbing factors. The factors underlying this impaired performance may even appear antagonistic to each other, such as abnormal distractibility and abnormal fixation; isolation of functioning and diffuse spread of functioning; perseverative rigidity ("inability to shift") and lability. It is to be hoped that the foregoing has helped to clarify the interrelationships of these factors by considering them together within the general context of the figure-ground syndrome.

BIBLIOGRAPHY

1. Goldstein, K.: The Organism, New York, American Book Co., 1939.
2. Klapper, Z. S., and Werner, H.: Developmental deviations in brain-injured (cerebral-palsied) members of pairs of identical twins, Quart. J. Child Behavior 2:288–313, 1950.
3. Rubin, E.: Visuell wahrgenommene Figuren, Copenhagen, Gyldendal, 1921.
4. Strauss, A. A., and Werner, H.: Disorders of conceptual thinking in the brain-injured child, J. Nerv. & Ment. Dis. 2:153–172, 1942.
5. Werner, H.: Perceptual behavior of brain-injured, mentally defective children, Genet. Psychol. Monogr. *31*, 1945.
6. Werner, H.: Development of visuo-motor performance on the Marble-Board test, J. Genet. Psychol. *64*:269–279, 1944.
7. Werner, H.: Abnormal and subnormal rigidity, J. Abnorm. & Social Psychol. *41*:15–24, 1946.
8. Werner, H.: Thought disturbance with reference to figure-background impairment in brain-injured children, Confinia neurol. *9*:255–263, 1949.
9. Werner, H., and Bowers, M.: Auditory-motor organization in two clinical types of mentally deficient children, J. Genet. Psychol. *59*:85–99, 1941.
10. Werner, H., and Strauss, A. A.: Types of visuo-motor activity in relation to low and high performance ages, Proc. Am. A. Ment. Deficiency *44*:163–168, 1939.
11. Werner, H., and Strauss, A. A.: Pathology of figure-background relation in the child, J. Abnorm. & Social Psychol. *36*:236–248, 1941.

The Developmental Nature of Pachyonychia Congenita

A Twenty Year Study of a Case

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Pachyonychia congenita is a rare congenital anomaly originally described under this title by Jadassohn and Lewandowsky.[1] According to Ormsby and Montgomery,[2] it is characterized by dystrophic changes in the nails, palmar and plantar hyperkeratosis, anomalies of the hair, leukoplakia, follicular keratoses of the acneform type, particularly about the elbows and knees, and dyskeratosis of the cornea.

In 1947 Wright and Guequierre[3] published a report of 2 cases with studies on therapy. One of these cases, a boy, entered the Temple University Hospital in 1936 at the age of 6, and he has been under constant observation up to the present time. Between June 1942 and June 1945 there was a total of six admissions to the Temple University Hospital, varying in length from a few days to several weeks. In 1942, the picture presented was as follows: The skin was generally dry and thickened, with many elevated lesions resembling keratotic plugs, particularly over the shoulders, elbows, and knees. The feet had denuded, crusted patches extending from the soles up the medial and lateral aspects. Removal of the crusts revealed reddened bases having a shiny or somewhat glazed appearance. The hair was dry and lusterless. The buccal mucosa and tongue showed patches suggestive of leukoplakia. Most striking were the changes in the nails. The nails of the fingers and toes were greatly thickened, some to a depth of 0.5 inch (1.2 cm.). The growth of the nail appeared to be away from the nail matrix rather than from the nail root (fig. 1).

The patient and his parents were chiefly interested in therapy for the crusted inflammatory patches and the nails. Because of the overgrowth of the nail plate, he was able to make but little use of his fingers. Wet dressings of buffered cysteine hydrochloride, as described by Goldberg,[4] were continuously applied to the crusted areas, and within 10 days all lesions were healed. (It is worthy of note that during subsequent recurrent outbreaks of these inflammatory crusted lesions, various other applications were tried, but invariably it was necessary to use the buffered cysteine hydrochloride to bring about healing.)

A consultation with a member of the surgical staff, Dr. George Rosemond, was requested, and the decision was reached to remove the nail plates completely with the patient under general anesthesia. This was done Nov. 17, 1942, and the patient was sent home. In June 1943 the patient returned, showing only a partial recurrence of the thickening of the nail plates but with recurrent erosive and crusted lesions on the feet. These again cleared completely with wet dressings of buffered cysteine hydrochloride solution.

In October 1944 the patient returned, showing regrowth of all the nails to about

FIG. 1. Fingernails prior to operation, showing marked thickening.

one half of their original thickness. As it was realized that the only method of completely stopping the growth of the nail would mean complete removal of the matrix, which in the condition is apparently the root from which the nail grows, it was decided in consultation with Dr. Rosemond to remove completely the tip of one finger as a trial method of therapeusis. Obviously such a procedure would result in a finger completely lacking a nail (fig. 2).

The next admission to the hospital was in February 1945, and this time the boy requested that the same procedure of removing the distal phalanges be used for all the fingers and the thumb of the right hand, as he had had no discomfort in the one finger and could use it for the first time in his life. The operation was performed with the patient under general anesthesia. In June 1945 the same procedure was carried out on the left hand, the operation having been almost completely successful on the right hand. Apparently a small amount of matrix was not removed from the middle finger, and it resulted in a slight regrowth of the nail (fig. 3).

The results of the operation in which a sufficient amount of the distal phalanx was removed to prevent regrowth of the nails have been remarkable. After complete healing, use of the fingers became possible to an extent that the boy was able to button his shirt for the first time in his life and was able to take piano lessons.

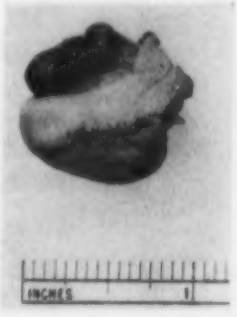

FIG. 2. Removed portion of the distal phalanx of the finger.

FIG. 3. Appearance of the fingers in 1956.

Now grown to manhood, he is a student in the Osteopathic Medical School and plans to specialize in pathology.

From time to time denuded areas of skin have appeared but have been limited to the soles, which also show areas of hyperkeratosis. By trial and error he has determined that wet dressings of Burow's solution in 1:10 dilution will heal the denuded areas and soften the hyperkeratotic areas to an extent that they are easily scraped off.

SUMMARY

A case of pachyonychia congenita, previously reported, is reviewed after 20 years of observation.

Surgical removal of a sufficient amount of the distal phalanx to prevent regrowth of the nails changed fingers that were previously incapacitating into useful digits.

BIBLIOGRAPHY

1. JADASSOHN AND LEWANDOWSKY. *In:* NEISSER, A., AND JACOBI, E.: Ikonographia dermatologica, Berlin, Urban and Schwarzenberg, 1907.
2. ORMSBY, O. S., AND MONTGOMERY, H.: Diseases of the Skin, ed. 8, Philadelphia, Lea & Febiger, 1943.
3. WRIGHT, C. S., AND GUEQUIERRE, J. P.: Arch. Dermat. & Syph. 55:819–825 (June) 1947.
4. GOLDBERG, L. C.: Arch. Dermat. & Syph. 36:331–377 (Aug.) 1937.

A Nutritional Approach to Growth Failure in Children

A Preliminary Report

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One of the most vexing problems encountered in pediatric practice is the great number of children who fail to grow and gain weight properly. In our experience, in the great majority of such children, "organic" causes of growth failure—such as metabolic, endocrine, and congenital disorders, chronic infection, and overt malnutrition—may readily be excluded as causative factors. In most instances, the failure to gain weight is the direct result of simple anorexia, which, in turn, appears attributable to failure to develop satisfactory eating habits.

Analysis reveals that many such children exhibit personality traits of a particular pattern. Whereas their behavior pattern remains well within the normal developmental limits, casual observation detects ample evidence of irritability, hyperexcitability, and allied minor disturbances. These, in turn, lead to the development of poor eating habits and an unsatisfactory appetite pattern. It is characteristic of such children that they are difficult to bring to the table at the appointed regular hour; they fidget and merely "pick at their food" and are impatient to leave the table before finishing their meal.

Recently, we were afforded the opportunity to inquire into the cause and treatment of anorexia and growth failure in a series of 56 infants and children ranging in age from 1 to 11 years. In this group, the symptoms shown in table I were observed. If uncorrected, these traits lead to failure to gain weight properly or even to actual loss of weight. However, in the absence of any organic disturbance, the rate of growth may readily be restored to normal by the development of proper eating habits and stimulation of the appetite.

Hitherto, treatment of such children has posed a difficult challenge. Thiamine has been extensively advocated to overcome anorexia, and vitamin B_{12} has been used with success to stimulate growth and weight gain.[1, 2, 5, 6] Crump and Tully[2] have presented data showing that the combination of vitamins B_1 and B_{12} effectively stimulates weight gain and growth. Nevertheless, many hyperexcitable and irritable children remain resistant to such treatment as a result of its failure to correct the basic cause of their profoundly disturbed appetites and eating habits.

Early and subsequent studies on reserpine have documented the effectiveness of this drug as an ataractic agent. Tenseness, irritability, and hyperexcitability are significantly reduced. Pertinent to the field of immediate interest have been the frequent observations that treatment with reserpine is often accompanied by a weight gain that cannot always be attributed to water retention. Talbot[4] successively employed small doses of reserpine in the treatment of irritable and hyper-

TABLE I

Symptoms Observed in 56 Children with Anorexia and Failure to Gain Weight

Symptoms	Percentage of children with symptoms
Anorexia	100
Underweight	52
Frequent colds	12.7
Crying spells	10
Loss of weight, nervous, irritable, whining, nail biting	8.3
Restless, fear of height, blinking of eyes, excessively ticklish and talkative, constant fatigue, uncooperative	6.4
Masturbation, insomnia, cranky, explosive speech, moody, enuresis, gagging of throat	4.2
Stubborn, "dawdles," feels cold	2

excitable infants and children and commented on the significant weight gains in many of these as a concomitant of their increased appetites.

Although one might entertain some doubts as to the use of reserpine in children not labeled neurotic, in view of the fact that it can apparently be administered indefinitely in small doses of 0.05 mg. three times a day with no untoward symptoms,[7] it was decided to determine whether this drug might not effectively restore satisfactory appetites and eating habits by virtue of a reduction of irritability and hyperexcitability. Furthermore, in view of the already demonstrated value of vitamins B_1 and B_{12} in promoting growth, we undertook a study of the effectiveness of Somatovite.*

Fifty-six children, whose symptoms are listed in table I, were treated with one tablet of Somatovite three times a day for from 1 to 34 weeks with an average duration of 12 weeks. The most dramatic result was the marked increase in appetite in 55 of the 56 within one month or less. This was most obviously demonstrated by the fact that, for the first time, the subjects spontaneously expressed a desire for food, began to ask for it before the scheduled eating hour, and asked for second helpings.

The effect on weight gain is illustrated in tables II and III. In summary, 50 of the 56 exhibited significant weight gains with an average in the entire 56 of $2\frac{1}{4}$ pounds/12 weeks.

Significant improvements in behavior and personality patterns were also noted. Fifty of the 56 exhibited excellent and 4 others substantial improvement as evidenced by the following: irritability and hyperexcitability were reduced and there was improvement in school work; there was improvement in general behavior—they were less stubborn and more congenial and adaptable with family and friends; masturbation was inhibited or decreased and fatigue was eliminated; speech was improved—it was no longer halting or staccato; fear, undue talkativeness, and

* Kindly supplied by the Medical Department of the Purdue Frederick Co., New York. Each tablet contains: reserpine, 0.05 mg.; thiamine mononitrate, 10.0 mg.; vitamin B_{12} (crystalline), 10.0 μg.

TABLE II

Weight Gains in Ounces /Week of Children Treated with Somatovite

Age (years)	No. of subjects			Weight gains		Duration of treatment (weeks)		Side effects
	Total	Male	Female	Average	Minimum and maximum	Average	Minimum and maximum	
1	1	0	1	5.1		8		None
2	3	2	1	6.5	2.0-8.7	6.7	3-14	None
3	9	4	5	3.8	0-7.3	11	3.5-29	None
4	2	0	2	−0.2	−4.0-3.6	7.5	4-11	None
5	9	5	4	2.8	0-6.0	9	1-18	None
6	8	6	2	2.5	0-9.0	14.8	4-25	None
7	8	4	4	4.5	1-9.2	16	4.5-34	None
8	5	2	3	6.1	2.2-8.0	13	5-22	None
9	5	1	4	3.5	1.0-7.3	12.3	5.5-27	Occasional stuffy nose in 1 female
10	3	1	2	1.8	0-3.0	14	5-19	None
11	3	2	1	7.7	5.5-10.4	13	9-19	None

moodiness were reduced. A marked improvement in sleeping pattern was noted: the children went to sleep on time and did not awaken during the night.

An unexpected observation was an apparent increase in nonspecific resistance evidenced by a decreased frequency of colds and improved general health and appearance.

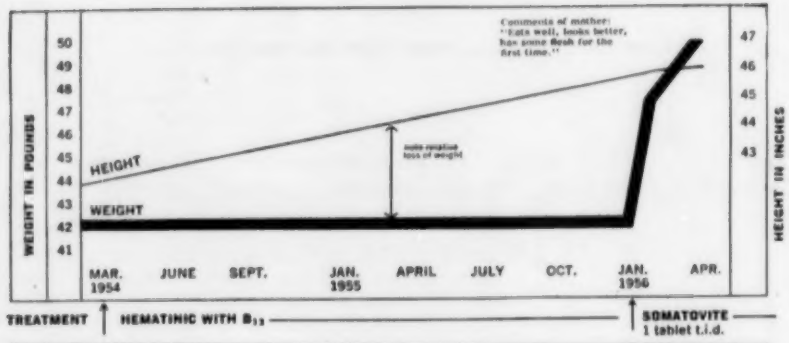
The beneficial effects of treatment were emphatically demonstrated in a number of children who had previously failed to improve on other forms of therapy. In our experience to date, Somatovite has proved more effective in stimulation of appetite and promotion of weight gain and growth than any other treatment devised for this purpose. Typical cases illustrating the favorable response to Somatovite are presented in figures 1 and 2.

Although Somatovite has now been given daily for periods up to 34 weeks, substantially no side effects have been noted even in infants 1 and 2 years of age. No instance of oversedation or water retention was encountered. Apparently, the dosage of reserpine in Somatovite has been satisfactorily adjusted to yield the de-

TABLE III

Effect of Body Habitus on Weight Gains (Ounces /Week) of Children Treated with Somatovite

Body habitus	No. of subjects			Age groups (years)	Average weight gain
	Total	Male	Female		
Normosome	22	14	8	2-11	4.4
Leptosome	19	11	8	3-10	4.0
Asthenic	15	2	13	1-11	2.9



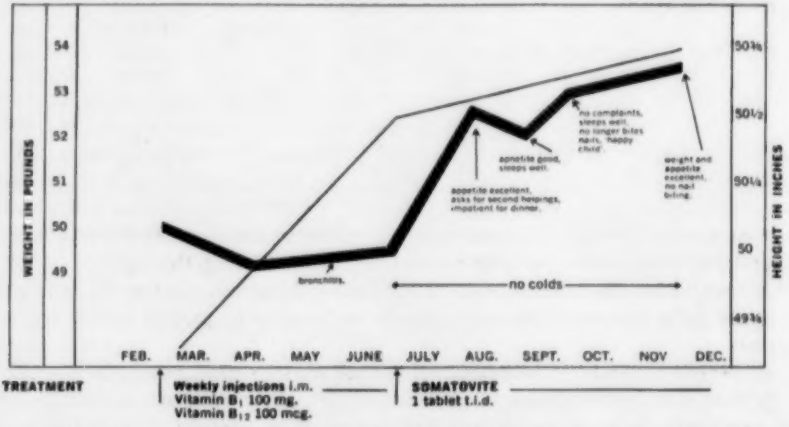


Fig. 1. (Top.) Effect of Somatovite on 8 year old girl with chief complaints of poor eating habits, no weight gain.

Fig. 2. (Bottom.) Effect of Somatovite on 8 year old girl with chief complaints of anorexia, failure to gain weight, nail biting, frequent colds, recurrent bronchitis.

sired therapeutic effect with no risk of toxic reaction. Experience to date indicates that the drug is both effective and safe.

The observations reported above are being extended and will be described in more detail in a subsequent paper.

SUMMARY AND CONCLUSIONS

1. Failure of children to eat and gain weight properly may often be attributed to irritability and hyperexcitability, which interfere with establishment of proper appetite and eating patterns.

2. The effect of Somatovite, containing small doses of reserpine to reduce irritability and hyperexcitability plus the growth- and appetite-stimulating vitamins B_{12} and B_1, was evaluated on a group of 56 children exhibiting anorexia, failure to

gain weight, and symptoms of mild behavior problems falling within the range of so-called "normalcy."

3. Excellent results were obtained from this method of treatment. Appetites increased promptly and substantial weight gains occurred along with improvement of the general behavior pattern. In many instances such effects were noted in children previously resistant to treatment with other medications commonly used to stimulate appetite and growth.

4. Continuous administration of Somatovite for periods extending up to 34 weeks revealed no evidences of serious toxic manifestations.

BIBLIOGRAPHY

1. Chow, B. F.: Sequelae to the administration of vitamin B_{12} to humans, J. Nutrition *43*:323–343 (Feb. 10) 1951.
2. Crump, J., and Tully, R.: The use of partial vitamin supplements in the treatment of growth failure in children, J. Pediat. *46*:671–681 (June) 1955.
3. Larcomb, J. W.; Perry, C. S., and Peterman, R. A.: Dietary supplementation of vitamin B_{12} in prepuberty school-age children, J. Pediat. *45*:70–74 (July) 1954.
4. Talbot, M. W., Jr.: The use of reserpine (Serpasil) in irritable and hypertonic infants, Ann. New York Acad. Sc. *61*:188–197 (April 15) 1955.
5. Wetzel, N. C.; Fargo, W. C.; Smith, I. H., and Helikson, J.: Growth failure in school children as associated with vitamin B_{12} deficiency—response to oral therapy, Science *110*:651–653 (Dec. 16) 1949.
6. Wetzel, N. C.; Hopwood, H. H.; Kruechle, M., and Gruenınger, R. M.: Growth failure in school children; further studies of vitamin B_{12} dietary supplements, J. Clin. Nutrition *1*:17–31 (Sept.-Oct.) 1952.
7. Wilkins, R. W.: Clinical usage of Rauwolfia alkaloids, including reserpine (Serpasil), Ann. New York Acad. Sc. *59*:36–44 (April 30) 1954.

Dr. Albert H. Holland, Jr., Appointed Clinical Consulting Editor of Antibiotic Medicine & Clinical Therapy

Albert H. Holland, Jr.

The Editors of Antibiotic Medicine & Clinical Therapy, Henry Welch, Ph.D., and Félix Martí-Ibáñez, M.D., are honored to announce that starting with the June issue Albert H. Holland, Jr., M.D., Medical Director of the Food and Drug Administration, will join their editorial board as Consulting Editor. In this role Dr. Holland will be primarily responsible for scientific selection and editing of all material relating to clinical therapy.

Dr. Holland was formerly on the editorial board of the *Journal of Southern Research*.

Prior to his appointment as Medical Director of the Food and Drug Administration on March 31, 1954, Dr. Holland was Medical Director of The Armour Laboratories in Chicago. Before joining Armour in July, 1950, he was Director of the Office of Research and Medicine at the Oak Ridge (Tenn.) Operations of the Atomic Energy Commission. He also served as Medical Adviser to the Manhattan Engineering District project at Oak Ridge, having been assigned originally by the Army as Medical Liaison Officer. Dr. Holland's service at Oak Ridge covered a period of approximately four years, from 1946 to 1950. Dr. Holland received his medical degree from the New York University College of Medicine in 1944, interned in the New York Post-Graduate Hospital, held an Assistant Residency at Memorial Hospital for Cancer and Allied Diseases, and was Resident in Internal Medicine at the Post-Graduate Hospital. He is the author of a great many scientific papers and is a distinguished medical lecturer.

We welcome this dynamic personality who will bring to AM&CT a wealth of clinical knowledge, editorial experience, and an understanding of the wide national problems of the chemotherapeutic field.

The Editors are also pleased to announce that with the June issue the scope of AM&CT will be enlarged to include, in addition to the present material on the clinical use of antibiotics, original papers, abstracts, news, and advanced reports on the clinical use of all chemotherapeutic agents, such as the sulfonamides, vitamins, hormones, tranquilizers, and others.

The Editorial Board will be enlarged accordingly to include distinguished figures in all branches of American and international medicine.

On Pediatrics

The symposium on children's diseases published in this issue may remind us that while the young have always been with us they have not always received their share of attention from the medical profession. The specialized branch of pediatrics is a comparative newcomer in the field, so new, it would seem, that the 1955 edition of the *Shorter Oxford English Dictionary* does not include the term in its 2515 pages, though *Webster's Dictionary* does.

The evolution of pediatrics reflects the attitude of peoples and historical periods toward children, and it epitomizes the history of mankind's humanitarianization from the primitive practices of infanticide to the modern medical reverence toward the child.

In Mesopotamia and Egypt, infanticide of normal children was abandoned. Later, pediatric advice is found in the Hippocratic "Aphorisms," although physicians of his time were rarely consulted about infants. Celsus spoke about "aphtha," rashes, and tonsillectomy. One of the earliest physicians to devote some care to human progeny was Soranus of Ephesus (early second century), who, notwithstanding his somewhat fanciful notions on the female genitourinary system, laid down excellent rules for the welfare of infants. His directions for treating the eyes of the newborn infant, for nursing, weaning, diet, and care of infantile diseases would not shock a modern pediatrician. In his time and later, when the infant was sick the nurse was treated, allowing her wine and *zythum*, or Egyptian ale.

Arabic pediatrics interdicted wine to children, but still neglected infants. During the Renaissance we find a number of works on the care of children, beginning with Paolo Bagellardo's *Libellus de aegritudinibus infantium et de morbis puerorum*, printed in Padua in 1472, and a German work by Bartholomaeus Metlinger, *Regiment der jungen Kinder*, published in Augsburg in the following year. The next century saw a mild rash of pediatric treatises, with Lobera de Avila's *Libro del regimiento de la salud . . . y de las enfermedades de los niños* in 1551, Soriano's *Modo y orden de malas enfermedades de los niños* (1600), Vallambert's *De la manière de gouverner les enfants dès leurs naissance*, and the "Father of English Pediatrics," Thomas Phaer's, *Boke of Children*, published in London in 1545. We must also consider Pérez de Herrera's book on garrotillo, or Spanish diphtheria, a disease immortalized by Goya. In the seventeenth century, the best known works were Blankaart's *Ziekten der Kinderen* (Amsterdam, 1684) and the pupil of Sydenham, Walter Harris', *De morbis acutis infantum* (London, 1689), which is said to have "attained a reputation far beyond its merits and was quoted and requoted for at least a hundred years."

The eighteenth century was peculiarly sterile in anything resembling pediatric specialization, although some attention was paid to the fate of thousands of ragged and unwanted children in that allegedly enlightened epoch. The foundling system, which was the greatest measure against infanticide, was then introduced in France.

Only in the next century did the care of children begin to develop as a branch of medicine, beginning with Credé's (1819–1892) introduction of ocular instillation of silver nitrate to prevent ophthalmia neonatorum. Germany took a lead in pediatrics with Heubner's (1843–1926) calculation of infant diets on the basis of their caloric values, and the treatises and lectures of Henoch (1820–1910) and Gerhardt (1833–1902). Escherich, the famous discoverer of the colon bacillus, took time off to study the bacterial flora of nurslings and their modifications in disease. Yet, in this same century the novels of Dickens reveal the hardships of children in England.

England and France were somewhat slower in developing pediatric knowledge, two landmarks in those countries being Rilliet's publication of a pioneer treatise on pediatric diseases in 1843 and the founding of the Hospital for Sick Children in London in 1852. The name of Edward Jenner (1749–1823) will always be revered in pediatrics. The palm for the founding of pediatrics in the United States is usually awarded to Abraham Jacobi (1830–1919), who lectured on pediatrics at the College of Physicians and Surgeons from 1857 and founded the first American pediatric clinic three years later.

In our own time, it might be colloquially claimed that children never "had it so good." The erstwhile ravages of congenital syphilis are well conquered in most Western countries, infantile tuberculosis is under control, and most childhood diseases, such as diphtheria, scarlet fever, and whooping cough, are no longer a serious menace. Two outstanding pediatric triumphs in our century are the treatment of rickets and the cure of cretinism due to thyroid insufficiency. The imminent conquest of poliomyelitis will be the crowning achievement in contemporary pediatric medicine.

The symposium presented in this issue takes us a few steps forward. We are assured by Dr. Craig that many of the congenital anomalies of the newborn, such as cleft palate, can now be corrected by skillful surgery. Dr. Kugelmass is reasonably optimistic that the new psychochemotherapeutic agents are valuable aids in treating behavioral disorders in children, notably in the mentally deficient. Cerebral palsy continues to baffle cure, though Dr. Deaver notes excellent progress in supportive care and rehabilitation techniques. Another congenital disorder, Mongolism, is discussed by Dr. Parmelee, who admits that while no medical treatment is of proved value, much can be done for these unfortunates to adapt them to a fairly normal family or social milieu.

We are left with one troubling aspect of future generations. Scientists warn us on all hands that the development of atomic power immeasurably increases the danger of genetic damage through radiation, either by producing larger numbers of malformed children or through harmful mutations. It would be irony indeed if all the devoted care that is given to the young by patient pediatricians were to be vitiated by a proliferation of little monsters. The present symposium should make it abundantly clear that while pediatric medicine is today performing wonders for children, it cannot overcome the frequent political stubbornness of adults.

Preliminary Study on the Use of Hydroxyzine in Psychosomatic Affections

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The physician is often consulted by patients whose illnesses are caused or further complicated by emotional stress. Effective management of these disorders cannot begin until the stress-producing stimuli are removed or the threshold of tolerance to the stimuli has been raised to a level where reactions are within normal limits and peace of mind is restored.

The ideal corrective measure, from the standpoints of economy and expediency, would be removal of the stress-producing stimuli. The medical literature records many instances where rapid remission of peptic ulcer, for example, has occurred after patients had changed occupations, had taken vacations long overdue, or had solved familial problems. The number of these fortunate individuals is low, percentagewise; the vast majority of troubled patients are forced to live with their stimuli, either by the pressure of circumstance or because a clear delineation of these stimuli is obscured by interlocking complexity. Thus, the physician is faced with two alternatives: (1) he can guide his patients to the development of a philosophic attitude toward the stimuli, as they are recognized, by psychotherapy, or (2) he can insulate his patients against the stimuli by drug therapy. The latter alternative is the easiest, quickest, and safest approach.

Choice of a drug to induce emotional calm should proceed according to the following criteria: (1) it should produce a therapeutic response rapidly, (2) it should be effective in the majority of cases, (3) it should not produce addiction, (4) toxicity should be minimal in the therapeutic range, (5) incidence of secondary effects should be low, (6) tolerance (resistance) should not develop with continued use of the drug, (7) it should be suitable for inpatient and outpatient therapy, and (8) it should not dull the senses, decrease perception, or interfere with mental acuity. Investigation of the drug hydroxyzine (Atarax*) was conducted on the basis of these criteria.

CHEMISTRY

Hydroxyzine is designated chemically as 1-(p-chlorobenzhydryl)-4-[-2-(2-hydroxyethoxy) ethyl] diethylenediamine. The hydroxyzine contained in the Atarax tablets and Atarax syrup used in this study was the dihydrochloride salt, the structural formula for which appears in figure 1.

The chemical structure of hydroxyzine indicates that it is related to a group of antihistaminic substances identical with respect to their basic benzhydryl and piperazine configurations.[1] Synthesis of hydroxyzine has created special pharmacodynamic properties that differentiate it from preparations of similar structure.

* The trade name of J. B. Roerig and Company (Division of Chas. Pfizer & Co., Inc.) for hydroxyzine is Atarax.

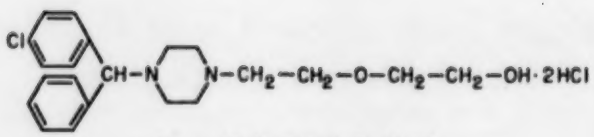

Fig. 1. Hydroxyzine hydrochloride

Pharmacologic studies have shown that it has remarkable sedative properties, an effect that points to its possible usefulness as an ataraxic drug. The sedation produced by hydroxyzine, slightly different in character and much greater in intensity than that found as a common side effect of antihistaminic drugs,[2] thus becomes a basis for all the drug's therapeutic indications. On the other hand, its antagonistic effect on histamine has aroused very little interest.

PHARMACOLOGIC STUDY ON ANIMALS

A simple examination of the behavior of animals subjected to the action of hydroxyzine was sufficient for an evaluation of its basic pharmacodynamic action.

Rats treated with hydroxyzine became quiet within a short time, their movements became slower and steadier, they assumed the most suitable position for undisturbed repose, and maintained this posture as long as they were left undisturbed. However, as soon as they felt some threat from the outside, they immediately fled from the danger, without loss of their customary agility and alertness.

Acute toxicity tests on 50 rats showed that the LD_{50} of intravenously administered hydroxyzine was 70 mg./Kg. A 1 per cent solution, *p*H 5, injected within one minute into the saphena vein, caused agitation among the animals; however, with a dose of 30 mg./Kg., this symptom was not observed. In acute oral toxicity tests on 50 rats, the maximum dose tolerated was 850 mg./Kg.; the average, 690 mg./Kg.

In chronic toxicity tests among rats, 5 animals withstood daily injections of 10 mg./Kg. for 30 days without mortality. Oral administration of 100 mg./Kg. in 5 rats produced no mortality over 30 days; 4 out of 5 rats withstood daily feedings of 200 mg./Kg. over a period of 30 days.[3]

CLINICAL METHODS

Hydroxyzine was administered by the oral route only. Coated tablets containing 25 mg. of hydroxyzine dihydrochloride or a syrup containing 2 mg./cc. was administered in daily dosages that varied, according to the patient, from 25 to 100 mg. Selection of the individual dose required adjustment to the proper degree of sedation, since the individual requirement did not seem to depend on the age, sex, or body weight of the patient. As an illustration, an initial daily dose of 25 mg. was reduced to 10 mg. for proper sedation of a robust adult weighing 198 lb., whereas in a 5 year old child, the same initial dose was raised to 100 mg. for proper sedation, without any untoward effect. In general, the hyperemotive and restless patients with animated movements were given large doses without experiencing troublesome incidents. As the hyperactivity decreased, the dosage was gradually adjusted downward to a

maintenance dose. On the other hand, patients with less severe symptoms were given small doses initially that were then increased as required to reach the therapeutic level, or decreased to an even lower level if somnolence or depression developed.

Hydroxyzine was administered to a group of 96 patients: 54 male and 42 female. Ages ranged from 2 to 93 years, and the duration of treatment varied from one week to two and one-half months. Patients were selected in several different categories of psychic and somatic disorders in order to determine the areas of psychosomatic medicine in which hydroxyzine would be most useful. In the group of patients with psychic manifestations, the drug was used in states of anguish and anxiety, in psychogenic insomnia, in infantile neuroses, and in states of senile excitation. Somatic manifestations were represented by circulatory, respiratory, and digestive disorders, as well as menopausal disorders, muscular aches and pains, and pruritis. Separation of these two broad classifications was not clear-cut. Most patients with manifestations of anxiety also complained of organic disorders; therefore, classification of the disorders was based on the one that appeared to be most prominent.

Six normal persons, serving as controls, received hydroxyzine in high enough doses and for a sufficient number of days to determine the normal physiologic effects of the drug.

CLINICAL RESULTS

The clinical results of this preliminary study are presented in table I. In view of the wide variety of clinical types represented and the shortness of the observation period, the over-all results shown in the table may be somewhat misleading. In spite of these limitations, the table may be useful as a check list of areas in psychosomatic medicine where hydroxyzine may be therapeutically beneficial.

A brief summary of some clinical cases assigned to the various groups may serve as a key to the clinical results with hydroxyzine.

Psychic Manifestations. Patients suffering from crises of anguish due to emotional shock generally responded favorably to the treatment; the same was true of patients with anxiety neuroses of long duration.

For example, 1 patient, after being subjected to a reducing cure that caused him to lose about 30 lb., underwent an intense episode of anxiety neurosis, accompanied by great restlessness and constant excitation. Psychotherapy combined with hypnotic sedatives did not yield the anticipated results. Hydroxyzine quieted the patient from the very first day, his insomnia disappeared, and shortly afterward the pathologic manifestations ceased completely.

In a group of children and older persons, the response was satisfactory. It is interesting to note that tolerance to the drug was excellent, even in cases where the patients were given relatively large doses. An explanation for this phenomenon was the great emotional tension present in these patients at both extremes of the age scale.

Circulatory Manifestations. Although nearly all the patients suffering from anguish and anxiety complained of palpitations and of an oppression around the heart, classification in this group extends only to those patients who indicated circulatory disturbances as the principal reason for their consultation.

One patient suffered from frequent attacks of paroxysmal tachycardia as the result of emotional irritation. Normal heart rhythm was restored with hydroxyzine, and the tachycardia did not recur during the two months in which he continued treatment.

TABLE I

Therapeutic Results with Hydroxyzine

	No. of cases	Satisfactory	Average	Inadequate
1. *Psychic manifestations*				
Temporary anguish neuroses	9	6	2	1
Permanent states of anxiety	12	7	3	2
Infantile neuroses	5	5		
Senile excitation	7	7		
	33	25	5	3
2. *Somatic manifestations*				
Circulatory				
Neurocirculatory asthenia	14	7	4	3
Tachycardia	5	3	1	1
Psychogenic arterial hypertension	2	2		
	21	12	5	4
Respiratory				
Bronchial asthma	4			4
Vasomotor rhinitis	1	1		
	5	1	0	4
Digestive				
Spasm of the esophagus	2	1	1	
Duodenal ulcer	2	2		
Peptic pseudo-ulcer	3	3		
Nervous dyspepsia	7	4	2	1
Mucous colitis	6	4	1	1
	20	14	4	2
Endocrine				
Menopausal disorders	9	6	2	1
Cutaneous				
Generalized pruritus	1		1	
Pruritus vulvae	2	2		
	3	2	1	0
Miscellaneous				
Feeling of unbalance	2	2		
Muscular aches and pains	2	1	1	
Facial tics	1	1		
	5	4	1	0
Total	96	64	18	14

An episode of psychogenic hypertension manifested itself in the case of the director of an institution when he was informed of the theft of a million pesos.* His arterial pressure rose to 220/110 mm., while for three days, excitation, anguish, and insomnia prevented him from taking any action in the matter. With 50 mg. of hydroxyzine, however, insomnia and anguish disappeared and he was able to act in a balanced and moderate manner. His blood pressure returned to normal within a few days after institution of treatment with the drug.

Respiratory Disorders. Hydroxyzine proved to be completely ineffective in 4 adult asthmatic patients. Its only usefulness in this connection was in modifying the insomnia and palpitations that were experienced as the result of adrenaline injections.

Digestive Disorders. A woman of 40 years was suffering from extensive dilatation of the esophagus and regurgitations as a result of spasm of the cardia, without detectable organic lesion. She had been treated previously by dilatations and hypnotic sedatives, but without favorable result. Upon daily administration of 75 to 100 mg. of hydroxyzine, the regurgitations began to disappear and she was thus able to swallow and retain nearly all foods. At the end of five weeks, her weight had increased by 7.7 lb. A new roentgen-ray study revealed a slight improvement, which was not in accordance with the patient's impression of being practically cured. This occurred at the time a new anxiety crisis set in, resulting in reappearance of the symptoms, although in diminished intensity. When treatment was resumed, the manifestations were brought under control.

A patient suffering from a duodenal ulcer that had been detected by roentgenogram was placed on the usual diet with antacids for a period of two months, but the epigastric pains persisted despite this treatment. At the time, the patient experienced great vexations and emotional problems that had to be solved. Upon treatment with 75 mg. of hydroxyzine per day, the epigastralgia as well as the hyperacidity disappeared.

Satisfactory results were also observed in other patients exhibiting a similar clinical syndrome and in whom the gastric ulcer was no longer apparent at the time of the follow-up roentgen-ray examination.

The most interesting results in this group of diseases of the digestive apparatus were undoubtedly those obtained in a number of cases of chronic mucous colitis, which showed very pronounced improvement with hydroxyzine treatment, after having undergone various previous examinations and treatments with no previous improvement.

Menopausal Disorders. On a number of occasions, the effectiveness of the product was demonstrated in circulatory and nervous disorders connected with the female climacteric, i.e., when used in conjunction with hormone treatment.

Pruritis. A young girl of 18, shortly before her scheduled marriage, was afflicted with intense pruritus vulvae, with eczematous lesions aggravated by scratching. Cortisone derivatives produced poor results. Administration of hydroxyzine caused the pruritus to disappear within one hour, and the effect lasted for eight hours, at first, and then for six hours on the following days. Administration of the product

* U. S. equivalent: $80,000.

at this interval was continued for two weeks, and the patient recovered without suffering a subsequent relapse.

Miscellaneous Symptoms. Included under this heading are 2 patients with nervous conditions who experienced a feeling of unbalance or nausea and in whom good results were obtained with this product.

For a period of two years, an extremely nervous patient had insistently complained of a pain in the back and in the nape, as if due to muscular rheumatism. Hydroxyzine was tried for two months, and the symptoms disappeared without further relapse, although they were replaced by other psychosomatic manifestations when treatment was interrupted.

The case of a 5 year old child with a facial tic is interesting because of the perfect tolerance of the drug in relation to the patient's weight. With a dose of 25 mg., the child's restlessness only increased and the tic did not begin to disappear until a dose of 100 mg. was used, without resulting in any observable prolongation of sleep or decrease in play activity.

Toxicity. No manifestations of toxicity were noted during the period of observation with the doses used. The effects described in table II must be attributed to the product's physiologic effects rather than to any toxic phenomena. None of the patients developed euphoria; on the contrary, it was noted that they were better able to judge reality at its true value, and there is therefore no reason to expect that the product may cause a mania in any condition.

DISCUSSION

The most constant effect exhibited by hydroxyzine was neurosedation, a state for which Delay et al[4] have proposed the term "neurolepsy." This state is characterized by diminished nervous and psychic tension, followed by tranquillity and peace of mind. Hydroxyzine, unlike such drugs as the barbiturates, bromides, and chloral hydrate, produces a calming effect without hypnosis. The sequence of events in this new pharmacologic activity is neurosedation first, followed by release from muscular

TABLE II

*Side Effects Reported by Patients in This Study**
(In Descending Order of Frequency)

Description	Occurrence
1. Increased intestinal peristalsis	Frequent
2. Mild rhinorrhea	Occasional
3. Increase in appetite, weight gain	Infrequent
4. Unsteadiness	5
5. Muscular weakness	3
6. Temporary constipation	2
7. Flatulence, tympanism	1

* In patients reporting side effects, these secondary effects usually were multiple; hence, two or more of the above effects may be covered by 1 patient's report.

tension; as tension vanishes, normal sleep is made possible. These three steps in the action of hydroxyzine will be discussed separately.

Sedation. Of the 96 patients observed, 95 confirmed the sedative effect. In only 1 patient was there an occurrence of excitation, the reverse of the usual reaction. This was the case of a nurse who exhibited excitation, arterial hypotension, and tachycardia one-half hour after taking the first 25 mg. dose. In hyperemotive patients presenting symptoms of anguish and anxiety, the drug produced a more favorable state of calm and tranquillity than any drug previously used. The patients did not lose interest in their customary activities but lost only their exaggerated response to external stimuli, and they were able to appraise the importance of these factors with serenity.

The intellectual state of the patients underwent no change, as demonstrated by the fact that 4 patients used their free time playing chess, dominoes, and cards—stating that they had won their respective games more easily under the effect of hydroxyzine because they played with greater self-assurance, forgetting their affective, financial, and professional preoccupations. On the other hand, in healthy persons to whom the product was administered and in many patients who were not suffering from excitation but rather from psychic depression, the feeling experienced as a result of sedation was annoying and disagreeable.

Relaxation of Muscle Tone. A sensation of asthenia or lassitude resulting from the relaxation of muscle tone, in the most widely varying degrees of intensity, was spontaneously referred to by half of the patients treated. Some of them declared that, although they felt the strength of their muscles had remained intact, they required a definite amount of mental effort in order to execute movements.

Others stated that their eyelids felt heavy and that they had a feeling of weakness in the facial muscles. Some experienced paresthesia, which they compared to the feeling of little drops of cold water or to mild itching. The foregoing sensations were described as pleasurable.

In 2 patients, the relaxation was observed objectively by the fall of the upper eyelids and by the absence of facial expression, denoting mild muscular asthenia. When the patients voluntarily closed their eyes, the lids could be lifted easily with the finger, in accordance with the method described by Thévenard.[5] The anti-nicotinic effect of hydroxyzine was noted by some of the patients who were habitual users of tobacco, this as a result of the muscular hypotonia, which neutralized the increase in muscle tone due to the nicotine.

Induction of Sleep. As a direct consequence of the effects referred to above, i.e., calmness and muscular relaxation, sleep set in more easily to the extent that the patient was relaxed in bed and sheltered from the effects of noises and external excitations.

When the doses used were higher than those required by the patient's nervous tension, diurnal somnolence set in, indicating a need for reducing the dosage and, occasionally, for interrupting the treatment. The sleep induced by hydroxyzine was generally nocturnal and similar to physiologic sleep, slightly prolonged in time. Dreams and nightmares decreased in a satisfactory proportion of cases. The drug's effect on insomnia of psychic origin was generally greater than that produced by

barbiturates. Night terrors ceased entirely in the case of 2 children, and somnambulism vanished in that of another. The principal characteristic of the sleep induced by hydroxyzine was its complete reversibility and the fact that the patients awoke as easily as they usually did.

The pharmacologic effects of hydroxyzine as clinically demonstrated in its three components, i.e., sedation, relaxation of muscle tone, and induction of sleep, seemed to be more intense at the start of treatment and to grow weaker on successive days, as if there were some acquired tolerance on the part of the organism. The serenity persisted, however, with continuing treatment.

It would be useful to know, from the anatomic point of view, the site at which hydroxyzine exerts its effect. This point of the drug's action should be studied experimentally in connection with another product, chlorpromazine, which exerts a similar effect on the central nervous system. Hiebel et al[7] succeeded in localizing the site of action of chlorpromazine in the reticular formations of the brain stem.

Recent physiologic research has shown that control of the states of wakefulness and sleep, control of neuromuscular tone, and also control of the tone of the sympathetic nervous system are dependent on the electrical activity of the reticula. If we extend these data to hydroxyzine, in view of its pharmacologic similarity to chlorpromazine, we might conclude that hydroxyzine also depresses the activity of the said reticular functions, thereby accounting for the effects, mentioned above, that are put to good use in the treatment of psychosomatic diseases.

Mechanism of the Psychosomatic Manifestations. The nerve centers are in constant communication with the deep organs by means of the nerve fibers, which are traversed by the emotional impulses. Emotions of all kinds, regardless of whether they originate in the external world in the form of physiologic or psychic traumas, or whether they are generated in the inner world by memories or by the imagination, are consciously picked up by the cerebral cortex. The energy contained in these emotions is derived in the form of nervous impulses descending, through separate stages, from the cortex to the peripheral endings of the sympathetic nervous system that penetrate into the visceral tissues.

The persistent increase in cortical dynamism causes the appearance of conditioned reflexes, compelling the neurons to unite with each other in different ways in order to form new, more easily traversable pathways, along which the emotional excitations preferably travel. When the nervous impulses are transmitted with ordinary frequency and via appropriate fibers, the functions of the organs stimulated are physiologic. But when the excitations reach the viscera with excessive frequency and are received by nervous pathways of recent formation, the functional alteration is manifested by the morbid symptoms of psychosomatic affections.

With overly intense and repeated excitations, structural changes make their appearance in the tissues, and the disease, which was functional at the outset, is transformed into an organic disorder. Conversely, when the nervous impulses are deficient and travel at a reduced frequency—as the result of a reduction in cortical dynamism—pathologic symptoms of a functional nature likewise make their appearance.[8]

Most synthetic antihistaminic substances block the passage of nervous stimula-

tions.[9] Hydroxyzine, by virtue of its chemical formula, belongs to this group and is useful only in the treatment of affections involving an increase in emotional tension. It has no effect where the psychosomatic manifestations are the result of psychic depression; the latter conditions call rather for treatment with a stimulant.

Treatment of the above diseases may be approached from the psychologic point of view; an attempt is made, through the use of psychotherapy or such physiologic means as stimulants and depressors of the nervous system, to modify the activity of the cerebral cortex.

Nearly all drugs that act on the nervous system occasionally produce inverse reactions that are the opposite of the ordinary reactions, and for this reason it is advisable to watch closely patients being treated with hydroxyzine.

Comparison of Hydroxyzine with Chlorpromazine and Reserpine. In the course of treatment, administration of hydroxyzine was alternated, in some patients, with that of another neuroleptic agent, thus making possible the following comparisons: (1) Chlorpromazine increased dreams and nightmares, it altered the number of pulsations by increasing or decreasing them, and it produced orthostatic hypotension. (2) From the point of view of the digestive apparatus, dryness of the mouth and a decrease in intestinal peristalsis were noted with chlorpromazine. However, chlorpromazine had other effects, such as blocking the vomiting and hiccup reflexes and other desirable properties, specific to this substance. (3) In equal doses, the neurosedative effect of hydroxyzine was superior to that of chlorpromazine; clinically, hydroxyzine caused no disturbance in the regulatory mechanisms of circulation and, in general, did not exhibit the sympathetic action of chlorpromazine. (4) Reserpine was likewise free of any sympathetic action but its absorption was very slow and it accumulated in the organism. It had a pronounced hypotensive effect and led to bradycardia. Sedation was more inconstant than with hydroxyzine.

CONCLUSIONS

An effort should be made to isolate the factors affecting the satisfactory tolerance of hydroxyzine. Two factors probably are involved: emotional tension and individual sensitivity.

The first of these factors seems to be basic, since it was observed in the present series of cases that: (1) the majority of the restless and agitated patients—with increased emotional tone—tolerated hydroxyzine satisfactorily and that the psychosomatic symptoms improved; (2) in a group of healthy persons whose emotional tone was normal, the sedative effect of hydroxyzine was described as disagreeable; (3) the patients suffering from psychic depression derived no benefit from the treatment and exhibited troublesome reactions.

In order to determine whether hydroxyzine therapy would be useful, it is necessary to judge the degree of intensity of the nervous and psychic tension, keeping in mind the fact that all cases showing improvement—even though apparently involving very dissimilar diseases—can be reduced to a common denominator, i.e., hyperemotivity. Selection of the cases to be treated depends on clinical and paraclinical study, and on an examination of the patient's personality.

The most constant pharmacologic effects of hydroxyzine are neurosedation, induction of sleep, and muscular relaxation; the best therapeutic results are observed in conditions accompanied by nervous excitation, insomnia, and muscular hypertonia. The first two symptoms can be ascertained by questioning the patient; since the increase in muscle tone is closely related to affective tone, it can be revealed in the movements, positions, and attitudes of the patient.

Hydroxyzine seemed to satisfy all the criteria of an ideal ataraxic drug for use in nonpsychotic hyperemotivity and tension: that is, (1) it produced the desired therapeutic response rapidly; (2) it was effective in sedation of the majority of patients (94 out of 95); (3) continued use did not seem to create dependence on the drug; (4) toxicity was negligible; (5) side effects were minimal; (6) resistance to the drug did not develop (although the period of study was rather short); (7) it was suitable for outpatient and hospital use; and (8) it had no deleterious effect on the senses or on mental acuity. Last, hydroxyzine can be used as a kind of pharmacologic test for measuring the degree of emotional tension.

SUMMARY

1. Hydroxyzine (Atarax) favorably modified psychosomatic manifestations when they were caused by an increase in emotional tension. In states of excitation, anxiety neuroses, and arteriovisceral conditions, the therapeutic results obtained were often much more favorable than those produced by other therapies.

2. Two other drugs, chlorpromazine and reserpine, exerted the same basic action as hydroxyzine, i.e., conservation of the state of consciousness with concomitant nervous sedation. Among the patients to whom these drugs were administered alternately, many exhibited more satisfactory results with hydroxyzine. However, chlorpromazine and reserpine are important in other clinical applications where hydroxyzine is ineffective.

3. The effect of hypnotic sedatives in moderate doses is irregular and inconstant. In strong doses, such as those used for sleep cures in psychosomatic medicine, there is danger of intoxication and the treatment cannot be prolonged for more than two to three weeks. With hydroxyzine, on the other hand, a neuroleptic treatment can be safely carried on for several months, since the drug is extremely low in toxicity and gives results that are comparable and sometimes superior to those obtained with other drugs.

4. If hydroxyzine treatment is interrupted after a short period of one or two months, manifestations of the disease reappear with less intensity. It may therefore be hoped that its administration for a sufficiently long period will be able to restore functional regularity in some patients.

5. The dosage of hydroxyzine must be adjusted initially in order to find the proper level of effectiveness. Variations in the patient's feelings and emotional tone necessitate such adjustments, which are deducible from observation of the patients during the course of treatment.

6. For control of nonpsychotic hyperemotivity and tension, hydroxyzine appears to be the drug of choice.

BIBLIOGRAPHY

1. Gaik, D. S., and Ducey, J.: Chemical structure of substances effective in treatment of parkinsonism, Arch. Int. Med. *85*:285–298 (Feb.) 1950.
2. New and Nonofficial Remedies, Philadelphia, J. B. Lippincott Co., 1953, p. 3.
3. Toxicity data (unpublished): Medical Department, J. B. Roerig & Co.
4. Delay, J.; Deniker, P.; Tardieu, Y., and Lemperiere, T.: Medicaments et cures neuroleptiques en thérapeutique psychiatrique. Premiers essais de la réserpine (Neuroleptic drugs and treatments in psychiatric therapy. First trials with reserpine), Presse méd. *63*:663–665 (March 4) 1953.
5. Thévenard, A.: Le diagnostic clinique rapide de la myasthénie (Rapid clinical diagnosis of myasthenia), Presse méd. *63*:21–22 (Jan. 8) 1955.
6. Ajuriaguerra, J., and Badaracco, J. G.: La thérapeutique de relaxation en médecine psychosomatique (Relaxation therapy in psychosomatic medicine), Presse méd. *61*:316–320 (March 4) 1953.
7. Hiebel, G.; Bonvallet, M., and Dell, P.: Action de la chlorpromazine au niveau du système nerveux central (Action of chlorpromazine in the central nervous system), Semaine d. hôp. Paris *30*:2346–2353 (June 6) 1955.
8. Thomas, J. E.: The autonomic nervous system in gastrointestinal disease, J. A. M. A. *157*:209–212 (Jan. 15) 1955.
9. Rackemann, F. M.: Allergy—Histamine and ACTH: A review of the literature 1948–1950, Arch. Int. Med. *87*:598–621 (April) 1951.

IN THE JUNE ISSUE OF

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BOOK REVIEWS

Psychopathology and Education of the Brain-Injured Child. Volume II. Progress in Theory and Clinic. ALFRED A. STRAUSS AND NEWELL C. KEPHART. New York and London, Grune & Stratton, Inc. 1955. 266 pages. $6.00.

To the pediatrician who often has a major role in the planning and management of a child with cerebral palsy, epilepsy, or mental retardation, this book is of special interest. Today the neurologic and orthopedic examinations, together perhaps with an electroencephalographic record, dominate the physicians' evaluation of the brain-injured child. Inasmuch as damage to the growing brain rarely fails to involve some portion of the neural elements essential to learning, familiarity with the psychologic disorders that can result is essential to a complete medical study.

Without becoming lost in the vocabulary of the basic sciences, these authors begin with a presentation of the pertinent aspects of neuroanatomy, neurophysiology, and embryology. Growth is shown to result in a constantly changing relationship of each part to the whole, so that symptoms from a damaged brain are related not only to the location of the insult but also to the moment in the developmental timetable at which the insult occurred. It is this characteristic that distinguishes brain injuries of children from those of adults. Subsequent chapters are devoted to an analysis of the development of perception, language, concept formation, and behavior in the normal individual, along with descriptions of the psychopathology found in those with brain damage. A separate chapter reviews the special testing techniques for recognizing specific psychologic disabilities in children with no gross impairment of over-all intelligence. Of direct practical value is the section in which preliminary conclusions are drawn affecting techniques of education. Although a sincere effort has been made to integrate knowledge in the fields of embryology, physiology, and psychology, the book would be a much greater contribution had there been a fuller presentation of the various neuropathologic entities and the psychopathology associated with them.—*Charles Kennedy, M.D.*

Diseases Affecting the Vulva. ELIZABETH HUNT. St. Louis, C. V. Mosby Co., 1954. Ed. 4. Pp. 236, illus. $9.00.

The new edition of this standard textbook on diseases of the vulva has been extensively revised since its first publication in 1940. While venereal diseases of the vulva have been thoroughly described by others, little attention has been paid in medical literature to nonvenereal affections. This handsomely illustrated book adequately fills the gap.

The author makes the valid point that the vulva is too often regarded as a genital organ rather than a part of the integument of the body as a whole. As a result, vulval affections are frequently given names that do not correspond to dermatologic conditions in other parts of the body; the use of the term "vulvitis" as a synonym for dermatitis is a case in point.

An interesting addition to the present volume is a chapter on herpes gestationis or

dermatitis herpetiformis of pregnancy. No specific treatment is known, though good results are reported with chlortetracycline and chloramphenicol. Hormone preparations of corpus luteum extracts and testosterone have also been found helpful.

The entire field is briefly though adequately covered, including sections on diseases of the vessels and glands, inflammations, psoriasis, lichen planus, leukoplakia, malignant and benign neoplasms, venereal diseases, parasitic and virus infections, and pruritus.

Vaginal Hysterectomy. LAMAN A. GRAY. Springfield, Ill., Charles C Thomas, 1955. Pp. 137, illus. $4.75.

The proponents of vaginal or abdominal hysterectomy have been at odds for a good many years. Each approach has had its vogue for a time. It is possible that Dr. Gray's monograph will swing the surgical tide in favor of the "vaginists" in pelvic surgery.

The book describes the author's personal technique which, as he states, was not learned in training but as the result of "observation, trial and error, and evaluation through a period of years." He lists indications for vaginal hysterectomy under three main headings: (1) complete prolapse of the uterus; (2) first and second degree prolapse with vaginal relaxation, and "combined syndrome"; and (3) some instances of uterine disease without relaxation. Cancer of the uterus is listed as the strongest contraindication. Adnexal disease, including inflammatory disease, endometriosis, and ovarian tumors, should be approached under direct vision and not through the vagina.

Surgical procedure is described in detail and admirably illustrated. Preoperative and postoperative care is also clearly delineated. The author recommends the prophylactic use of procaine penicillin (300,000 units) and dihydrostreptomycin, 0.5 Gm. twice daily for five days, followed by gantrisin, 1 Gm. four times daily, to control urinary tract infection. The author does not recommend the use of estrogens to thicken the atrophic vagina before surgery.

The Physician and His Practice. Edited by JOSEPH GARLAND. Boston, Little, Brown & Co., 1954. Pp. 270. $5.00.

This collection of essays by 18 authors provides a compact guide for those who are beginning a career in medicine. One section discusses the character and personality of the physician and his wife in relation to the family circle and to the wider responsibilities of community life. Other chapters are devoted to a discussion of opportunities, specialty practice, hospital work, laboratory facilities, medical supplies, and group practice.

A portion of this book that could well prove of value to established physicians is the one dealing with office organization, accounting practices, and investment policies. The various methods by which money can be saved in income tax and estate tax are outlined by a lawyer.

In that respect, a point made by the editor in his foreword may be quoted: "One of the great impediments to the establishment of good public relations in medicine

is that the physician too often fails to appreciate the importance of conducting the business of his profession in a clear and orderly fashion, acceptable to himself, to his patients, and to the tax collector."

Hemorrhage of Late Pregnancy. JOHN S. FISH. Springfield, Ill., Charles C Thomas, 1955. Pp. 180, illus. $5.50.

Hemorrhage of pregnancy, although considerably less frequent today than 10 years ago, is still the primary cause of maternal death in the United States, according to this author. By his definition, hemorrhage may be expected to occur in 1 of 20 patients in the average private obstetric practice.

Of this number, one third will be found to have placenta praevia, including low implantation, and an equal number will be found to bleed from rupture of the marginal sinus. Abruptio placentae is the cause of about 10 per cent of hemorrhages occurring during late pregnancy and labor. Other causes are lacerations of the cervix, circumvallate placenta, vasa praevia with rupture of a fetal vessel, rupture of a vulvar varix, and cervical carcinoma or polyp.

This book clearly describes the clinical characteristics and diagnosis of the various types of dysfunction. The section on treatment is perhaps not as comprehensive as might be expected but it is adequate. Macroscopic, microscopic, and roentgenographic illustrations add to the value of this monograph, as do the 14 case histories reported in an appendix.

Physicians' Office Attendants Manual. HENRY B. GOTTEN AND DOUGLAS H. SPRUNT. Springfield, Ill., Charles C Thomas, 1955. Pp. 93, illus. $3.75.

This is a useful and practical manual for young women wishing to train to be attendants in the office of physicians, dentists, and technical laboratories. While it is primarily intended for beginners, even employees with considerable experience can learn something useful from this volume.

The section on office work includes information on keeping records, stenographic work and bookkeeping, hospital references, care of office supplies, narcotics, minor surgery, laboratory and x-ray studies, and basal metabolism tests. The section on laboratory work includes hints on the care of equipment, preparation of laboratory solution, urinalysis, sputum and blood examinations, and other useful and compact data. Even some physicians might appreciate this handy refresher course in everyday procedures.

NONPOLIO VIRUS TYPING. The University of Minnesota and eight other diagnostic laboratories offer a new diagnostic service in cases resembling poliomyelitis but that are due to nonpoliomyelitis viruses. The laboratories will give particular attention to the newly named ECHO viruses, a group containing 13 or more Enteric-Cytopathogenic-Human-Orphan virus types now under suspicion as etiologic agents in so-called nonparalytic poliomyelitis and aseptic meningitis.

RESEARCH ON CLEFT LIP AND PALATE. The U. S. Public Health Service has awarded a $14,000 grant to the Northwestern University dental school for research in cleft lip and palate. The grant will be used over the next three years for studies on growth and development of facial and head bones and muscles in 100 children from birth to 4 years of age.

NEW STOMACH CANCER TEST. The American Cancer Society reports that Dr. Robert J. Bolt at the University of Michigan is using the enzyme chymotrypsin in a new stomach cancer test. The enzyme digests the mucin in the stomach contents, making it easier to find cancer cells present when the gastric contents are studied under the microscope.

POSITIONS ABROAD FOR MD'S. The Division of International Health, U. S. Public Health Service, announces numerous openings for physicians in various international health programs in which the United States is participating. A two year service term is required; salary is commensurate with experience and qualifications. Details may be obtained from the Division of International Health, Public Health Service, Washington 25, D. C.

HEART RESEARCH. The American Heart Association has awarded $830,000 to 131 research scientists for cardiovascular research for one year beginning July 1. Studies will be conducted in 24 states, the District of Columbia, Great Britain, Greece, and Denmark. Another group of grant-in-aid awards will be announced by the Association later this year.

DETECTION OF PROSTATE CANCER. A promising method of early detection of cancer of the prostate gland by biochemical analysis of the saliva was described to members of the International Association for Dental Research, St. Louis,

at their annual meeting. The method involves the measurement of acid phosphatase in the saliva.

HORMONE TRIGGER FOR CORTISONE. Dr. Roger Guillemin, Baylor University College of Medicine, physiologist and neuroendocrinologist, has isolated a hormone from the hypothalamus that triggers the production of ACTH and cortisone. This substantiates Dr. Guillemin's theory that the hypothalamus regulates the endocrine system.

CARCINOMA CHEMOTHERAPY. A new agent, chloroquine mustard, derived from nitrogen mustard and the antimalarial chloroquine, was reported to the American Cancer Society. It combines the cancer-destructive activity of nitrogen mustard with the characteristic of chloroquine to localize in certain body tissues, permitting larger, more effective, and less toxic dosages of nitrogen mustard to attack the tumor sites.

HEART ATTACK DIAGNOSIS. Dr. Warren Wacker of Harvard Medical School has reported a new method of diagnosing cardiac dysfunction as early as four hours after onset. It is based on the discovery that there is a sharp increase in the activity of lactic dehydrogenase and malic dehydrogenase after cardiac failure, coupled with a decrease of zinc in blood serum.

LONGER POLIOMYELITIS IMMUNITY. Dr. Jonas E. Salk, director of the Virus Research Laboratory of the University of Pittsburgh Medical School, recently told the annual meeting of the Association of American Physicians that lifelong immunity from paralytic poliomyelitis might be achieved with vaccine. He declared that although cases of clinical poliomyelitis might continue, these would not reach the paralytic stage.

SEX HORMONE THERAPY. A Berlin physician reports that administration of high doses of sex hormones to patients with various types of tumors, severe reticulo-endothelial disturbances, brain function and optic function disturbances, and important organ destruction produced substantial improvement. Intramuscular testosterone was administered, combined with either follicle-stimulating hormone or estradiol. Treatment lasted up to nine months.[1]

MENTAL HEALTH FUND. A $125,000 mental health fund has been established by the Smith, Kline & French Foundation, Philadelphia, for use in the campaign against mental illness during 1956. Principal objectives of the fund will be basic research, psychiatric training, and professional and public education.

BIBLIOGRAPHY
1. Neuner, H.: Med. Monatschr. 10:97-100 (Feb.) 1956.

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FOREWORD

The objective of the QUARTERLY REVIEW OF OPHTHALMOLOGY is to bring together in one publication concise but authoritative abstracts of current articles on ophthalmology, according to an all inclusive plan which includes all special, state, and national journals as well as the bulletins of clinics, hospitals, etc., and the transactions of meetings. This embraces both the domestic and foreign literature.

To assist the reader to locate quickly the articles of current interest all data are classified and published according to the following systematic plan:

- Anatomy, Embryology, Heredity, Development, and Nutrition
- Optics, Physiology, and Psychology of Vision
- Physiology, Chemistry, and Biochemistry of the Eye
- Pathology, Bacteriology, and Immunology
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- Anterior Chamber and Pupil
- Uveal Tract and Sympathetic Ophthalmitis
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A section entitled International Record of Ophthalmology is included at the beginning of the journal. The Record Section consists of advanced clinical and experimental reports.

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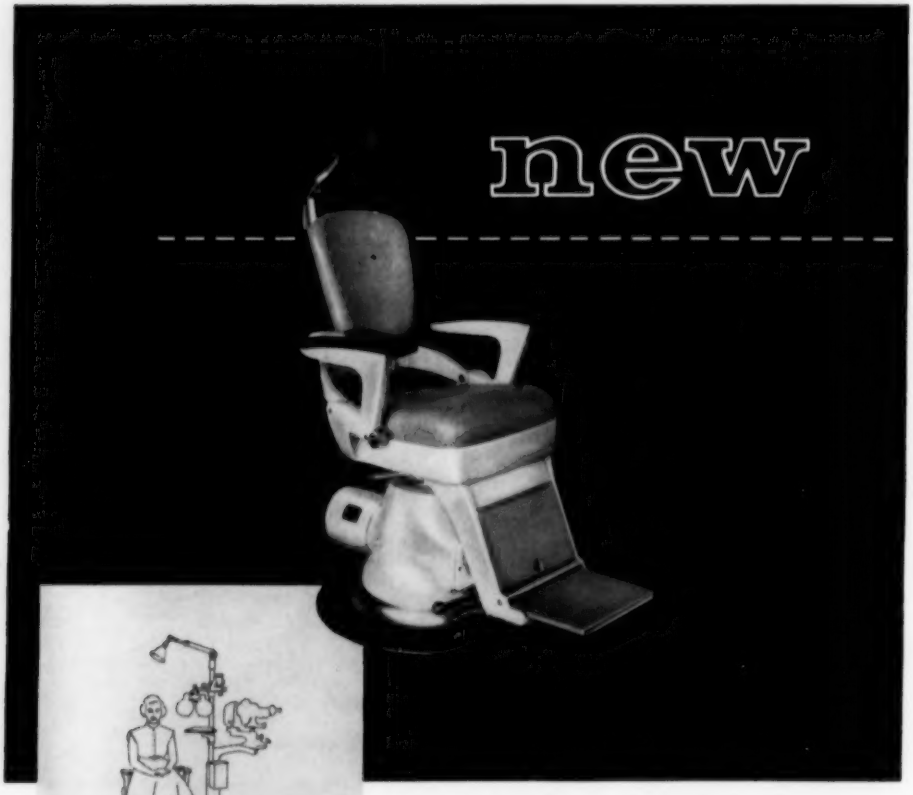

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SINCE 1853

Endogenous Uveitis*†‡

A Review of the General Physician's Role in Diagnosis and Treatment

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Part I

Living in an era of teamwork, alliances are formed in all fields of human endeavor. This is particularly true of the medical profession. Ophthalmologists have long been aware of the need to enlist the cooperation of their medical confreres in the fight against blindness.[1] In the present paper a plea is made for collaboration in combating one of the most important causes of blindness—endogenous uveitis. Through closer cooperation in making an accurate etiologic diagnosis, the resultant possibility of attacking the underlying cause will permit more effective treatment.

Continuous improvement in clinical and laboratory methods, based on intensive research by competent investigators, has broadened our understanding of uveitis in general. But there are still too many cases in which the etiology remains obscure, and consequently treatment is unsatisfactory. It is not surprising, therefore, that statistics covering a period of more than 10 years indicate no essential change in the percentage of blindness caused by uveitis.

Studies concerning the causes of blindness in the United States[2] in 1940 revealed that 11.5 per cent was due to uveitis. Statistics compiled by Cowan and English[3] in 1941 indicate that inflammation of the uveal tract was responsible for blindness in 18.3 per cent of these eyes. In 1946 Aylesworth[4] reported that approximately 14 per cent of 12,654 Canadian children and adults examined were sightless because of uveitis. In England and Wales more recent statistics by Sorsby[5] indicate that 7.95 per cent are blind as a result of this disease. Holst[6] in 1952 attributed approximately 10 per cent of blindness in Norway to uveitis. These statistics of blindness do not include those individuals who have lost one eye or whose visual acuity has been drastically reduced by uveitis.

* Aided by a grant from The Ophthalmological Foundation, Inc., and from the Department of Research, New York Association for the Blind.

† Read before the meeting of the graduate course in ophthalmology, Yale University School of Medicine, New Haven, Conn., May 28, 1954.

‡ The second part of this article will appear in the September issue of this journal.

CLASSIFICATION OF UVEITIS

Before discussing the problems involved in diagnosis and treatment of endogenous uveitis, a few general remarks on the classification of uveitis and the terminology are necessary.

Uveitis means inflammation of the vascular coat of the eyeball. Depending upon which part of the uveal tract is involved, iritis, cyclitis, iridocyclitis, or choroiditis may be present. Duke-Elder[7] distinguishes uveitis due to: "1. Exogenous infections derived from without. 2. Secondary infections affecting the uveal tract by continuity or arising from some ocular event. 3. Endogenous infections."

He says, "Endogenous inflammations, which are caused by the entrance by way of the blood streams of organisms or stray products into the eye from some source situated elsewhere in the body, form the majority of inflammatory conditions affecting the uveal tract."[7] This type of uveitis is the subject of the present paper.

Another classification of uveal inflammations having some clinical and pathologic justification divides uveitis into granulomatous and nongranulomatous types.[8, 9] The recognized causes of endogenous granulomatous uveitis are: syphilis, tuberculosis, brucellosis, sarcoidosis, toxoplasmosis, and certain fungus and virus infections. In this type of uveitis it is believed that the causative agent may actually be found in the uveal tissues, especially during the acute inflammatory stage of the disease. In the nongranulomatous type there is little evidence that living organisms are in the tissue of the eye, and the process appears to be one of an allergic reaction to a specific organism or its products in a sensitized tissue.

DIFFICULTIES IN DIAGNOSIS

A clinical diagnosis of uveitis usually presents little difficulty to the ophthalmologist, but he is greatly handicapped in establishing the etiology of this condition and is frequently forced to depend on clinical judgment rather than scientific facts in making the diagnosis. Unfortunately, the clinical appearance and course of the disease are only rarely pathognomonic. In the majority of cases, bacteriologic proof of exact etiology is lacking.

Verrey[10] and von Sallmann et al[11] occasionally found a positive aqueous culture in the early stages of the nongranulomatous type of uveitis. Murray,[12] in his study of 22 cases of nongranulomatous uveitis, reported only 1 positive culture, which probably resulted from contamination. Aqueous cultures made by Hogan and Thygeson[13] and by Berens et al[14] were sterile.

Even pathologic diagnoses may be inaccurate, as was demonstrated by Wilder.[15] Upon re-examining sections of human eyes previously diagnosed as tuberculous or possible tuberculous uveitis, she found 41 cases in which *Toxoplasma* organisms were identified. The proved causes of uveitis, as determined by the histopathologic studies of Wilder and Bickerton,* are shown in table I.

In many cases, several conditions may appear to be causally related to uveitis, thereby presenting a complex problem of differential diagnosis. For example, there

* Through the courtesy of Major John H. Bickerton and Mrs. H. Wilder, Armed Forces Institute of Pathology, 1953.

TABLE I

Endogenous Ophthalmitis, Proved Cases (Organisms Identified)

Organisms identified	No. of cases
Adult toxoplasmosis	58
Syphilis	2
Tuberculosis	10
Blastomycosis	2
Cryptococcus	3
Monilia	1
Leprosy	27
Nematode	28
Cysticercus	2
Mucor	1
Inclusion body	1
Organisms not found but diagnosis seems to be	
(a) Syphilis	124
(b) Tuberculosis	54
Brucellosis—no organisms found so far	
Granulomatous uveitis (cause undetermined)	100
Total	413

may be a positive Wassermann reaction, abnormal tuberculin sensitivity, *and* evidence of foci of infection in the same patient, each representing a disease capable of causing uveal inflammation.

THE ROLE OF THE GENERAL PHYSICIAN

The obvious lack of knowledge concerning the scientific diagnosis of uveitis leads to the conclusion that only the full cooperation of the general physician and of other specialists with the ophthalmologist may aid in establishing an etiologic diagnosis, so that specific treatment may be administered to patients suffering from uveitis. Only teamwork can increase the success of our fight against blindness and bring about a reduction in the loss of sight caused by uveitis.

The general physician and specialists in other fields should be alerted to all the pathologic conditions that may cause endogenous uveitis. Examinations, conducted with these special considerations in mind, should decrease the number of cases of uveitis with undetermined etiology. To facilitate this task, a survey sheet (fig. 1) for investigating patients with chronic infection has been used by us for many years.

A positive result of a specific test or examination in a patient rarely determines the etiology of the uveitis. It is the comparison of positive with negative results, the correlation of clinical with laboratory findings, and their critical evaluation in the light of accumulated experience that permit an approach to exactness in establishing the etiologic diagnosis of uveitis. Even with the greatest care, a presumptive diagnosis is all that can be made in the majority of cases. Therefore, the following includes not only a discussion of the nonspecific treatment applicable to all forms of

endogenous uveitis but also an evaluation of the clinical criteria upon which the etiology of uveitis is based. The role of the general physician does not end with the finding of the pathologic process responsible for uveal inflammation. His help is invaluable in managing treatment because he usually knows, from previous experience, the patient's reaction to drugs, his allergies, as well as special indications and contraindications for treatment.

NONSPECIFIC TREATMENT APPLICABLE TO ALL FORMS OF ENDOGENOUS UVEITIS

Local nonspecific measures include mydriatics, decongestants, and the application of heat. Their value may be questionable in affections of the posterior segment, but these therapeutic aids are beneficial in the treatment of any involvement of the

MEDICAL SURVEY SHEET AND CHRONIC INFECTION STUDY
THE OPHTHALMOLOGICAL FOUNDATION, INC.

Name Date

Medical Date Dr. B/P
ENT Date Dr.
Dental Date Dr.
Allergy Date Dr.
Dermatology Date Dr.
Urology Date Dr.
Gynecology Date Dr.
X Rays Date Dr.
Skull
Sinuses (Stereoscopic?)
Teeth
Chest
G. B.
G. I. tract
Blood: CBC: Hb RBC WBC Poly Lympho Eosino
Schilling I Mono Baso
Sed. Rate (Westergren, if other specify) C Reactive Protein
Chemistry: Sugar NPN Calcium Uric Acid A/G ratio
Cholesterol Urea Phosphorus Gamma Globulin
Bleeding Time Clotting Time Platelets Capill. Fragility
Serologic Tests: Syphilis Brucellosis Toxoplasmosis (Feldman Dye)
Skin Tests: Mantoux Brucellosis Toxoplasmosis
Frei Other organisms
Autogen. Vaccine (mixed?)
Lens Protein Uveal Pigment
Other allergens
Urinalysis
Feces (Blood, Ova, Parasites)
Basal metabolism Radio-active Iodine uptake PBI
Liver function tests: Cephaline Floc. Thymol Turbidity Other
Spinal Fluid
Smears and Cultures (Date and by whom)
Conjunctiva
Aqueous
Sinuses
Nasal
Pharyngeal
Tonsils
Gums
Gall Bladder
Cervix
Prostate
Urine
Feces
Blood

Diagnosis
Prognosis
Conclusion and Treatment Recommended

Signed

FIG. 1. Medical Survey Sheet for investigating patients with chronic infection.

anterior segment. However, mydriatics are certainly not contraindicated in most posterior affections, and their use facilitates a more careful observation of the active process.

It is now a well established fact that the topical use of corticosteroids is beneficial in controlling inflammatory affections of the anterior uveal segment. Either by instillation or by subconjunctival injection, these drugs quickly overcome inflammatory signs and symptoms and give the ophthalmologist the opportunity to employ more specific measures before irreparable damage is done to the vital structures. It is important to use these hormonal substances for a sufficient length of time since too early withdrawal may be associated with a recurrence that may prove to be more resistant to treatment than the original attack.

In inflammatory affections of the anterior segment that are resistant to local treatment with cortisone, and in all posterior uveal inflammations, systemic administration of cortisone, hydrocortisone, prednisone (Meticorten*), prednisolone (Meticortelone†), and/or corticotropin should be given a trial.

A survey of the results of the treatment of 669 patients with diseases of the uveal tract following the administration of ACTH and/or cortisone‡ indicates that 453 (68 per cent) responded favorably to the therapy and 215 (32 per cent) showed no improvement.

Duke-Elder et al[16] reported 4 cases of generalized chronic granulomatous uveitis treated with cortisone. The results in 2 cases were doubtful, 1 case improved following treatment, and there was no improvement in the fourth case. However, in nongranulomatous uveitis and in iridocyclitis and uveitis associated with spondylitis or rheumatoid arthritis, rapid improvement was apparent. Of a total of 91 cases of acute and chronic uveitis treated with ACTH and cortisone, there was improvement in 69 per cent.

Of 48 cases of choroiditis treated with ACTH and cortisone, improvement was reported in 73 per cent and there was no response in 27 per cent. The latter were usually the more advanced cases.

An evaluation of ACTH and cortisone therapy in 168 patients with iridocyclitis indicated improvement in 88 per cent. The results obtained in cases of first attacks of acute iridocyclitis correspond with the findings of Duke-Elder et al[16] and others. The patients usually improved rapidly, as did those with recurrent acute iridocyclitis. A number of the cases of subacute iridocyclitis showed rapid improvement, but the response was generally slower and less complete. In chronic iridocyclitis the improvement was usually slight and in many instances only temporary. Of 39 patients with iritis who were treated with ACTH and cortisone, 84 per cent showed improvement. Rapid improvement was noted in acute recurrent iritis and little or no improvement in chronic iritis.

The more recently available prednisone and prednisolone are in the process of evaluation. There are indications that these drugs may be more powerful than

* The trade name of Schering Corp. for prednisone is Meticorten.

† The trade name of Schering Corp. for prednisolone is Meticortelone.

‡ Statistics include our cases, those treated by eye surgeons of the New York Eye and Ear Infirmary, and some selected from the literature.

cortisone and hydrocortisone, and that the incidence of undesirable side effects may be lessened.

The local use of antibiotics by instillation, iontophoresis, and subconjunctival or retrobulbar injections is usually ineffective.

Other general nonspecific measures include shock medications, such as protein therapy in the form of milk and milk products, autohemotherapy, Piromen, typhoid vaccine, and typhoid H antigen. The authors prefer typhoid H antigen in an initial dose of 20 million organisms, repeated every three to four days until from four to six injections have been administered, increasing the doses by 10 to 20 millions, depending upon the reaction obtained. Following these injections, paracentesis is performed for the purpose of increasing the concentration of antibodies in the aqueous; it may be repeated several times on alternate days. Paracentesis is also of value in the temporary control of increased intraocular pressure.

TUBERCULOUS UVEITIS

Diagnosis. Ocular tuberculosis may assume widely different clinical pictures depending on the virulence of the organism, the degree of tissue hypersensitivity to tuberculous protein, and the resistance of the host. In general, the disease is characterized by a low grade inflammation, a prolonged chronic course with some remissions and exacerbations, but rarely entirely by quiescence. In a small number of cases the clinical picture may be almost characteristic, but in the majority of instances tuberculous uveitis is clinically indistinguishable from other forms of granulomatous uveitis or even at times from the nongranulomatous inflammations. (See figure 2.)

The diagnosis of tuberculous uveitis is usually based on indirect evidence, since a positive diagnosis based on bacteriologic studies of the intact eye is impossible. Among the criteria upon which the diagnosis of tuberculous uveitis is made are: (1) skin sensitivity to tuberculin, (2) the presence of a systemic focus or history of tuberculosis in other parts of the body, (3) focal reaction to tuberculin, (4) improvement of the ocular lesion under tuberculin therapy, (5) the exclusion of other possible etiologic factors, and (6) the clinical course of the disease. It has been reported[17] that the Middlebrook-Dubos hemagglutination test may prove to be of considerable value in the diagnosis of ocular tuberculosis, but more recent evaluations[18] have not confirmed these earlier suggestions.

There are no accurate statistics available regarding the prevalence of ocular tuberculosis because the criteria for the diagnoses vary greatly in different clinics and are often influenced by the personal opinion of the examiner. The correlation between the clinical and pathologic diagnoses reveals great discrepancy. One study[1] showed an error of 54 per cent. The statement by Duke-Elder[7] that "the clinical diagnoses of uveitis are obviously a matter of faith rather than fact" is certainly applicable to tuberculous uveitis. In a recent report, Thiel[19] attributed the etiology of 75 per cent of his uveitis cases to tuberculosis.

Therapy. The objectives of the more specific measures employed in the treatment of tuberculous uveitis are: (1) to increase general resistance; (2) to eliminate tissue allergy; and (3) to destroy the infecting organisms. The measures employed to

increase general resistance are nonspecific and consist of improving general health by rest, sunlight, fresh air, and adequate diet, and the elimination of any other systemic debilitating infections. For the elimination of tissue allergy, high dilutions of tuberculin, the strength depending on the type of reaction obtained, are used by subcutaneous injection over a long period of time.

A wide variety of drugs have been employed over the years in an attempt to destroy or attenuate the tubercle bacillus. The more promising drugs now in the process of being evaluated are streptomycin, dihydrostreptomycin (DHS), and *p*-aminosalicylic acid (PAS). PAS is currently being prescribed in divided doses of 12 Gm. daily with 0.5 to 1 Gm. of DHS intermittently every two to three days. The duration of treatment has not been established, but it should probably continue for a minimum of six weeks and in certain cases for several months. The patient should be carefully watched for evidence of untoward reactions. Isonicotinic acid hydrazide has been widely acclaimed as an effective antituberculous drug, but no conclusive reports of its effect in ocular tuberculosis are available. The recommended daily dose is from 3 to 5 mg./Kg. of body weight.

Cutler et al,[20] in a study of 61 tuberculous patients, suggested the simultaneous use of streptomycin, isoniazid, and *p*-aminosalicylic acid. It was believed that many patients are infected with multiple strains of *Mycobacterium tuberculosis*, some of which are resistant to a specific drug and sensitive to others. Before this form of treatment is instituted, the diagnosis should be clearly established, since there is no evidence that other forms of endogenous uveitis are benefited by these drugs. Recent investigations seem to show that the adrenal corticoids can be used in the treatment of tuberculous lesions of the eye in conjunction with antituberculous drugs with beneficial results, despite the fact that earlier reports in the literature contraindicated the use of these hormonal substances in any form of tuberculous infection.[21]

OCULAR TOXOPLASMOSIS

Toxoplasmosis is a disease that is more widespread than has been generally recognized. Approximately 76 cases of congenital toxoplasmosis with an associated chorioretinitis, in which the diagnosis was considered proved or probable, have been reported in the literature. As previously mentioned, Wilder[15] found *Toxoplasma* organisms in chorioretinal lesions that had been diagnosed as tuberculous. In connection with this latter finding, Hogan[22] has pointed out that other organisms are similar in shape and size to *Toxoplasma gondii*. Duke-Elder et al[23] have stated that coli and nuclear debris may be mistaken for *Toxoplasma* organisms and that caution should be observed in this respect. Certain organisms, studied by Jacobs,[24] are indistinguishable morphologically from *Toxoplasma* and require serologic tests to differentiate the forms. Therefore, there is doubt as to whether or not histologic examinations are adequate for establishing the diagnosis of acquired toxoplasmosis without recovery of the organisms after animal inoculation.

Recently, Jacobs et al[25] have seemingly confirmed Wilder's findings in a parasitologically proved case of toxoplasmosis in an adult. Certainly the bodies and

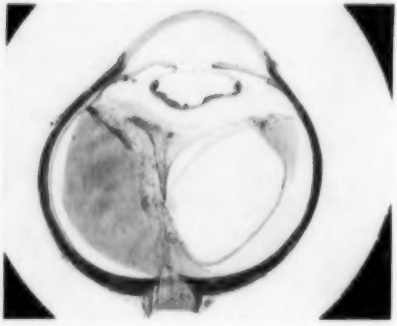

Fig. 2. (Left.) Ocular tuberculosis from a white woman with pulmonary tuberculosis. (From Wilder, H. C., and Bickerton, J. H.: Organisms identified in inflammatory lesions of eyes in the Registry of Ophthalmic Pathology, A. M. A. Arch. Ophth. 53:575–584, 1955.) Fig. 3. (Right.) Toxoplasmosis. Site of larva in vitreous membrane subretinal serous exudate. Retinal detachment. (From Wilder, H. C.: Nematode endophthalmitis, Tr. Am. Acad. Ophth. 55:99–109 [Nov.-Dec.] 1950.)

pseudocysts seen by one of us (C. B.) in Wilder's sections could not have been merely debris.

Toxoplasmosis occurs in three different forms, depending on the age of the patient; namely, congenital, that acquired during childhood, and the adult form.

Acute toxoplasmosis is a generalized infection involving virtually every organ of the body, although lesions may be only microscopic. The *subacute* form of toxoplasmosis is accompanied by regressive lesions in the extraneural viscera, whereas in the central nervous system and the eyes, toxoplasmosis continues to proliferate actively. *Chronic* toxoplasmosis may yield clinical and laboratory evidence with no signs of widespread activity. Chorioretinitis is the most frequent sign. (See figure 3.)

Diagnosis of Toxoplasmosis. Recent studies have shown that toxoplasmosis may attack any part of the uveal tract as well as other tissues of the eyeball. Thus, its importance in the etiologic diagnosis of uveitis has been established.

The involvement of the uveal tract occurs both in the congenital and in the acquired forms of the disease. In general, no distinctive clinical features are found in uveitis associated with congenital toxoplasmosis. A fairly characteristic type of chorioretinal lesion, seen in congenital toxoplasmosis, presents a more or less cicatricial form of retinochoroiditis, usually macular and almost invariably bilateral.

The following additional findings are of diagnostic significance: abnormal infantile and childhood development, both physical and mental, bilateral internal hydrocephalus, a variety of neurologic disorders, and intracerebral calcifications, revealed by careful roentgen-ray examination. Recently, some doubt has been cast on the specificity of the latter by Sabin and Feldman.[26] The symptomatology of the Sabin-Feldman syndrome closely resembles that of congenital toxoplasmosis, being characterized by chorioretinal lesions and encephalopathy. However, intracerebral calcifications occur in 5 per cent (in contrast to 90 per cent in congenital toxoplasmosis), and serologic and biologic tests for toxoplasmosis are constantly negative.

It has been reported[22] that in congenital cases an active retinochoroidal process may be found in the fundus simultaneously with cicatricial lesions. According to Hogan,[27] acute chorioretinitis due to congenital toxoplasmosis may appear as late as the twelfth and fourteenth years of life. This would indicate that the later appearance of toxoplasmic chorioretinitis does not exclude its congenital origin. Therefore, attempts should be made to differentiate sequelae of congenital toxoplasmosis from the acquired infection, both in children and in adults. Intracerebral calcifications are unknown in acquired toxoplasmosis.

New light has been thrown on the general symptomatology of the acquired form of toxoplasmosis. Several authors[28, 29] have reported lymphadenitis (mainly cervical) sometimes associated with papulomacular erythema and with lymphocytosis and mononucleosis as signs of acquired toxoplasmosis, thus necessitating the consideration of infectious mononucleosis in differential diagnosis.

Of the laboratory studies helpful in establishing the diagnosis of toxoplasmosis, serologic tests are the most essential. These include the dye test or cytoplasm modifying test (Sabin) for the detection of the *Toxoplasma* cytoplasm-modifying antibodies, which develop within 10 to 20 days and persist for at least five years on the same level (1:256 to 1:4000), and the complement fixation test. The complement fixation antibodies appear at a late stage and disappear early. Therefore, this test may be negative even during the most active stage of the infection.

In the interpretation of these tests, the high incidence of *Toxoplasma* antibodies in the normal population must be taken into consideration. The dye test alone is sufficient for establishing a diagnosis, except in infants during the first week of life when the complement fixation test is mandatory. The latter test alone can establish the diagnosis in the majority of patients with congenital toxoplasmosis. In early infancy, diagnosis is correct if antibodies are found in infant and mother in significant titers. Varying titers during the period of observation are most suggestive of an active stage of the disease.

According to Sabin et al,[30] the skin test with *Toxoplasma* antigen is of limited value because if negative, it does not exclude infection, and if positive, it does not differentiate between an old and a current infection.

Treatment of Ocular Toxoplasmosis. Although various drugs are capable of destroying the *Toxoplasma gondii* organisms in vitro, they have been found ineffective in vivo. Conversely, sulfonamides and sulfadiazine in particular, which are without effect on *Toxoplasma* in vitro, have given promising results both in experimental animals and in a few cases of human toxoplasmosis, especially when combined with the antimalarial agent, pyrimethamine (Daraprim*).[31]

* The trade name of Burroughs Wellcome & Co., Inc., for pyrimethamine is Daraprim.

ABSTRACTS

OCULAR MOVEMENTS AND MOTOR ANOMALIES, NYSTAGMUS, READING DISABILITY

25. *Correlation between Physiologic and Clinical Aspects of Exotropia.* ABRAHAM SCHLOSSMAN, New York, New York and S. ARTHUR BORUCHOFF, Boston, Massachusetts. Am. J. Ophth. *40*:53–64, July, 1955.

A total of 324 cases of exotropia were studied. Exotropia occurs approximately one third as often as does esotropia. The following classification for exotropia is recommended: intermittent exotropia; constant alternating exotropia; constant uniocular exotropia.

Intermittent exotropia constitutes 85 per cent of all cases of exotropia; the term refers to those cases that at times show manifest divergent strabismus and at times heterophoria, on the basis of temporal and spatial measurement of the squint.

Exophoria-exotropia is that condition in which, for any given distance of the object of fixation, the patient will at times show an exotropia and at times an exophoria of approximately similar degree.

The characteristics of the various subgroups of intermittent exotropia were studied from the points of view of measurements for distance and near and of near-point of convergence.

The incidence of myopia, emmetropia, and hyperopia parallels that of the general population.

Only 5 per cent of cases with intermittent exotropia are benefited by the correction of myopia, and here the effect is mainly on the measurement for near.

In intermittent exotropia it appears that fusion in the primary position is more likely to be "all or none" for distance fixation than for near: if present, it is more likely to be constantly present, or, if absent, to be totally absent. At the near measurement, fusion in the primary position is usually present or intermittent, and very rarely absent.

In 16 per cent of cases the deviation was greater for distance than for near; in 31 per cent approximately equal for distance and near; and in 53 per cent greater for near than for distance.

Although some cases fall into the classification of divergence excess and convergence insufficiency, the vast majority do not, and it is urged that the use of such categories be de-emphasized.

Constant alternating exotropia constitutes approximately 6 per cent of exotropia; such cases are similar to those of intermittent exotropia, except that fusion is weaker. Hence, the patient does not exhibit exophoria even part of the time.

Constant uniocular exotropia constitutes about 9 per cent of exotropia. It differs from the other two types in that the strabismus is probably secondary to amblyopia, since a well defined obstacle to clear vision in one eye can be demonstrated in most cases.

It has been shown that exotropia and esotropia differ fundamentally from the points of view of: (a) incidence in the general population; (b) percentage of incidence of the different types of esotropia and exotropia; (c) etiologic differences of the types; (d) relation of the strabismus to amblyopia; (e) the role of the refractive error; and (f) the role of heredity. 16 references. 8 tables.—*Author's summary*.

ANOMALIES OF REFRACTION AND ACCOMMODATION, CONTACT LENSES

26. *Myopia of Prematurity*. MARY C. FLETCHER AND SYLVAN BRANDON. Am. J. Ophth. *40*:474, October, 1955.

The development of the eye in 462 premature infants, 136 of whom had retrolental fibroplasia, has been studied over the past four years. These infants were found to have a high and fluctuating myopia during the neonatal period, more exaggerated in the small infants with immature eyes and in those infants who subsequently developed retrolental fibroplasia. Myopia observed early in retrolental fibroplasia may remain as a residual of the disease.

The mechanism for the production of myopia in premature infants appears to be associated with the immature eye and the underlying metabolic disturbance in retrolental fibroplasia. There probably exists an abnormality in metabolism of the media of the developing eye influenced by the abnormal extrauterine existence of the premature infant.

CORNEA, SCLERA, AND TENON'S CAPSULE

27. *Toxic Conjunctivitis Due to Antibiotics*. HELENA FEDUKOWICZ, GEORGE N. WISE AND MILTON M. ZARET. Am. J. Ophth. *40*:849–855, December, 1955.

A toxic reaction to antibiotics may develop immediately after short usage of the sensitizing drug or in a delayed manner following sensitization of the tissues prior to systemic or local use. It is well known that the conjunctiva takes part in the general sensitization in the body and that sensitizing the tissues of one eye may lead to sensitization of the other, or indeed of the entire organism. This sensitized tissue, after a latent exposure period of days to years, may suddenly develop an inflammatory reaction to various allergens.

For the past several years more than 100 cases of toxic conjunctivitis due to antibiotics have been studied both clinically and by means of laboratory procedure. The clinical picture of toxic conjunctivitis included sudden onset, redness and edema of the lids, moist eczematoid reaction of the skin of the lids, mechanical ptosis, bulbar and palpebral conjunctival injection, scanty or no purulent discharge, foreign body sensation, "dryness" of the eyes and even the throat, and headache, especially frontal. In spite of the dry sensation, abundant tearing was a most characteristic finding. The affection was mainly unilateral. Corneal complications were quite common, as were enlargement and tenderness of the preauricular lymph node on the involved side. The conjunctival scrapings showed the basophilic granules that occurred so typically in the monocytes. Some of these granules, especially very

dark and refractive, when free, or occurring in epithelial cells, were surrounded by a light zone and were highly suggestive morphologically of viral elemental bodies.

A careful history with date of onset, dates and types of medication, and subsequent course, together with the clinical and laboratory findings, usually leads to the correct diagnosis of toxic conjunctivitis. All cases had negative cultures or showed only saprophytic bacteria, especially *Bacillus zerosis*.

Finally, it cannot be stressed too strongly that the routine use of antibiotics for all types of conjunctivitis should be avoided. It is a serious error to sensitize an individual to an antibiotic unnecessarily and thus deny him its lifesaving effect in a later, more serious, general illness.

UVEAL TRACT AND SYMPATHETIC OPHTHALMITIS

28. *Uveitis in the Contralateral Eye following Cataract Extraction.* BERNARD KRONENBERG, New York, New York. Am. J. Ophth. *40*:205–209, August, 1955.

A form of uveitis is presented that develops in the unoperated eye following a cataract operation in the other eye. This uveitis must be differentiated from (1) sympathetic ophthalmia and (2) a coincidental uveitis. This is of utmost importance because the therapeutic approach for the three conditions is very different.

The syndrome reported consists of the following findings: (1) The operated eye does not show any inflammatory reactions. (2) There is no reduction of vision or change in function in the operated eye. (3) The unoperated eye shows a marked ciliary congestion. (4) The keratic precipitates in the unoperated eye are heavy and numerous. They are of the granulomatous type. (5) The onset of inflammation in the unoperated eye can occur after months or after many years. (6) The early removal of the lens in the unoperated eye leads to a rapid quiescence of the condition. (7) Nonintervention or late intervention leads to complete destruction of intraocular tissues and total loss of vision.

The pathogenesis of the condition is explained by the fact that the patient may be sensitive to lens substance as a result of the previous operation. The lens capsule of the unoperated eye may be slightly ruptured, and a small amount of lens substance may extrude to cause a violent reaction in the unoperated eye. This condition is a definite clinical entity.

The therapeutic approach stressed in this so-called lens-induced uveitis is the prompt removal of the lens in the second eye. This removal is advised on the face of an active inflammation. 5 references.—*Author's abstract.*

CRYSTALLINE LENS

29. *The Management of Monocular Cataracts.* EVERETT L. GOAR, Houston, Texas. A. M. A. Arch. Ophth. *54*:73–76, July, 1955.

Cataracts should no longer be allowed to go to maturity or beyond because vision remains good in the opposite eye. A mature or hypermature cataract is more difficult to remove in capsule than an immature one. When an eye is blind from cataract, convergence insufficiency develops, then exotropia. From this point on, it may be

impossible ever to attain binocular single vision again. Intumescent and hypermature cataracts are prone to cause secondary glaucoma. In a person in the active phase of life, a cataract should be removed when useful vision is lost; 20/100 might be used as a criterion. A contact lens may be worn. Patients get enough fusion to prevent diplopia and to hold the eye straight, and they have a full field of vision in the operated eye. 3 references.—*Author's abstract.*

RETINA

30. *Studies on the Visual Toxicity of Methanol.* ALBERT M. POTTS, JULIUS PRAGLIN, IRENE FARKAS, LOWELL ORBISON, AND DONALD CHICKERING. Am. J. Ophth. *40*: 76, November 1955.

The only consistent early change in sections of retinas from methanol-poisoned, bicarbonate-treated monkeys is cyst formation in the external nuclear layer. This is despite marked ophthalmoscopic, pupillary, and electroretinographic changes.

The only animal to show possible changes in the ganglion cell layer of the retina was one that survived nine days. This animal also showed demyelinization of the optic nerve.

Methanol-poisoned, bicarbonate-treated monkeys consistently showed edema and nuclear pyknosis in the basal ganglia, particularly the putamen and caudate nucleus.

When ophthalmoscopic edema and pupillary dilatation set in in these animals, the electroretinogram shows a large a-wave and no b-wave. The same picture may be reproduced with appropriate doses of formaldehyde and formate.

The bearing of these findings on our present knowledge of methanol poisoning is discussed.—*Author's abstract.*

NEURO-OPHTHALMOLOGY, OPTIC NERVE, VISUAL PATHWAYS, CENTERS, AND VISUAL FIELDS

31. *Ophthalmologic Changes Produced by Pituitary Tumors.* MAX CHAMLIN, LEO M. DAVIDOFF, AND EMANUEL H. FEIRING, New York, New York. Am. J. Ophth. *40*:353–368, September 1955.

One hundred and fifty-six cases of pituitary adenomas and craniopharyngiomas were analyzed as to the ophthalmologic changes produced. The three most common ocular findings were visual field defects, atrophy of the optic discs, and loss of central vision. All the other ocular changes such as extraocular muscle palsy, pupillary changes, papilledema, proptosis, and nystagmus occurred so infrequently as to be almost insignificant in their diagnostic value.

Of all the cases, loss of central vision occurred in 32 per cent, optic atrophy in 50 per cent, and bitemporal field defects in 86 per cent. Twenty-three of the cases were eosinophilic adenomas, and in these cases the incidence of the findings was not nearly as great as in the others. However, the acromegaly picture produced by eosinophilic adenomas is so diagnostic that one rarely has to lean upon the ophthalmologic findings to make a diagnosis. In those cases of chromophobe adenoma

and craniopharyngioma, on the other hand, the diagnosis may often depend to a great extent on the ophthalmologic findings; bitemporal hemianopia was found in 96 per cent of the chromophobe cases (109 cases) and in 100 per cent of the craniopharyngiomas (18 cases).

While the bitemporal defect was easily demonstrated in many of these cases, in some of them minimal techniques had to be used to bring out minimal defects.

Of the three outstanding ophthalmologic findings in pituitary tumors, loss of central vision, optic atrophy, and bitemporal hemianopia, the last-named visual field defect was most important, not only from the point of view of frequency, but because the bitemporal hemianopia accounted for the optic atrophy or the loss of central vision. In other words, the presence or absence of optic atrophy may be dubious depending on the examiner's interpretation of the discs. On the other hand, one cannot diagnose true optic atrophy unless a visual field defect exists. Similarly, whether or not central vision has been lost is often difficult to demonstrate, especially if the patient's usual central vision is not known. On the other hand, loss of central vision in these cases depends directly upon and is a result of the loss of paracentral field extending to include fixation. Therefore, of the three most frequently encountered signs of pituitary tumor, bitemporal hemianopia, optic atrophy, and loss of central vision, the single most outstanding and most important diagnostic sign is the bitemporal hemianopia.

Aside from the importance of picking up bitemporal hemianopia in its earliest stages, it is very important to differentiate the visual field findings of bitemporal hemianopia due to mass lesions from the visual field findings of retrobulbar neuritis, which may at times simulate visual findings of pituitary tumors. Careful techniques in visual field examination should help to make the differential diagnosis at a very early stage, thus giving the patient the optimum chance for recovery with surgery or radiotherapy as indicated. 11 references. 8 figures. 1 table.—*Author's abstract.*

GLAUCOMA AND HYPOTONY

32. *Phacolytic Glaucoma; a Clinicopathologic Study of One Hundred Thirty-eight Cases of Glaucoma Associated with Hypermature Cataract.* MILTON FLOCKS, San Francisco, California, C. STUART LITTWIN, Teaneck, New Jersey and LORENZ E. ZIMMERMAN, Washington, D. C. A. M. A. Arch. Ophth. *54*:37–45, July, 1955.

A study of 138 enucleated eyes with glaucoma associated with hypermature cataract establishes this type of glaucoma as a clear-cut clinical and pathologic entity. The name "phacolytic glaucoma" is proposed for this condition because it is descriptive of the basic pathology and because it serves to differentiate it from other types of lens-induced glaucomas, such as that associated with exfoliation of the lens capsule, intumescent cataracts, or spherophakia.

Liquefaction of the lens cortex is followed by degeneration of the lens epithelium and escape of the lens liquid into the anterior chamber. The lysed cortical material evokes a histolytic response. Macrophages swollen with phagocytized lens material block the filtration apparatus to produce acute glaucoma.

The clinical findings are highly characteristic. The onset of acute glaucoma in

a cataractous eye of an old person with good vision in the other eye (and particularly if the other eye is aphakic) should make one seriously consider the diagnosis of phacolytic glaucoma.

Comprehension of the pathology and pathogenesis of phacolytic glaucoma will inevitably lead to the correct treatment of this surgical emergency; namely, cataract extraction and irrigation of the anterior chamber. 15 references. 13 figures. 2 tables.—*Author's abstract.*

ORBIT

33. *Hemangiopericytoma of the Orbit.* SIDNEY A. FOX, New York, New York. Am. J. Ophth. *40*:786–789, December, 1955.

Hemangiopericytoma of the orbit is a rare vascular tumor. Of the 54 cases in the medical literature, only 3 have involved the ocular adnexa. Its importance lies in the fact that, unlike most vascular tumors, it is one of a small group (including the hemangioendotheliomas and the leiomyosarcomas) that may be malignant.

This tumor was first described by Stout and Murray in 1942. It originates by proliferation of the contractile pericytes, cells with long processes, which are found in the external capillary walls.

The case history of a 34 year old white woman who had a series of recurrences of this tumor in the right orbit is reported.

The presence of hemangiopericytoma should be suspected whenever an angiomatous neoplasm, however atypical grossly, shows tendencies to aggressive invasion and recurrence. 21 references. 2 figures.—*Author's abstract.*

MEDICAL OPHTHALMOLOGY

34. *Topical Use of Cortisone in Sympathetic Ophthalmia; Four-year Observation of a Successfully Treated Case.* L. L. FORCHHEIMER, New York, New York. Am. J. Ophth. *40*:248–251, August, 1955.

A review of the literature dealing with cortisone treatment of sympathetic ophthalmia is given. A case of a perforating eye injury due to a particle of steel lodged in the vitreous is presented. The perforating wound involved the iris and caused a traumatic cataract. Three operations were performed: magnet extraction of a particle of steel, extraction of a traumatic cataract, and removal of an iris prolapse.

A bilateral sympathetic uveitis developed, which was intensively treated with cortisone eye drops for a period of 11 weeks. The sympathetic uveitis cleared up completely, but recurred whenever cortisone medication was discontinued. Cortisone eye drops were then used twice a day for a period of three years.

The last corneal precipitates of the right eye disappeared three years after the original injury. No symptoms of sympathetic ophthalmia have developed during the two years since the cortisone medication was finally discontinued.

It appears, therefore, that this case of bilateral sympathetic ophthalmia was permanently cured by the exclusive local use of cortisone eye drops. 10 references.—*Author's abstract.*

TRAFFIC AND DRIVING PROBLEMS RELATED TO OPHTHALMOLOGY

35. *A System of Vision Testing for Motor Vehicle Drivers.* JOHN V. V. NICHOLLS. Canad. M. A. J. *74*:346–352, March, 1956, and Canad. Services M. J. *12*:215–226, March, 1956.

The following table gives the recommended visual requirements.

Recommended Visual Requirements

Type of license	Corrected visual acuity		Refractive error (eq. power)	Fields (horizontal)	Re-exam.
(1) Drivers of heavy transport	20/30	20/30	Not more than 4Δ	Full (140 degrees) each eye	Every 3 years
(2) Drivers of light transport	20/30	20/60	Not more than 5Δ	Full (140 degrees) each eye	Every 3 years
(3) Private drivers					
(a) Unconditional	20/40	20/100	Not applicable	Full (140 degrees) in one eye; not less than 100 degrees in other	Every 3 years
(b) Conditional	Monocular, strabismus, and cataract candidates licensed on their merits				

Since tests for stereopsis, color vision, and night vision are considered not feasible, or not to apply, they should be left out of the ocular examination. It is recommended that Snellen's test be used for testing visual acuity. 24 references.—*Clement McCulloch, M.D.*

36. *Discussion of Medical Aspects of Traffic Accidents.* L. BRODY. Canad. Services M. J. *12*:237–239, March, 1956.

There are no adequate criteria for the evaluation of visual performance in relation to driving. There are but inadequate or unreliable measures of the visual traits themselves. Performance is dependent on, or modified by, a great variety of external and internal factors. It is unrealistic, if not impossible, to separate the visual functions from the psychologic functions.

Standards for vision should vary somewhat according to the type of vehicle to be operated. There is a need for periodic visual examination of all drivers. This should be done every three years.—*Clement McCulloch, M.D.*

37. *A Survey of the Visual Problems Relating to Motor Accidents.* R. G. C. KELLY AND R. L. HALL. Canad. Services M. J. *12*:209–214, March, 1956.

A questionnaire was sent to the traffic authorities of all provinces in Canada asking for the provincial visual requirements for drivers and for any data that were available relating to visual efficiency and accidents. There were few data relating visual efficiency to accidents. The visual standards were found to vary greatly between the provinces. Three provinces had no visual requirement; one province

has an extremely complicated system relating the findings on the eye examination to the maximum allowable speed.

One of the causes of accidents at night is failure to reduce speed to adjust to the lighting conditions. The ability to see at night is cut down by alcohol, carbon monoxide, anoxia, and smoking cigarettes.

It is recommended that all provinces adopt the visual standards that are proposed by Dr. Nicholls, that all provinces set up a system of visual testing of all candidates for licenses and institute a periodic visual check of all drivers, that the visual facts thus obtained be available for statistical purposes, and that an educational campaign be conducted regarding the dangers of night driving. 11 references.—*Clement McCulloch, M.D.*

38. *Can Modern Visual Research Reduce Traffic Accidents?* P. W. MILES. Canad. Services M. J. *12*:227–236, March, 1956.

In conditions of fog, haze, or darkness there is a tendency to blurring of vision due to inability to relax the accommodation. This nearsightedness can be corrected with a −0.75 diopter lens, which will improve vision under those conditions. While visual acuity is extremely important, seldom is any object first discovered in the fixation area. This image first falls on the peripheral retina, attracting attention. The size of the peripheral field is therefore extremely important when considering the safety of drivers.

Skill of depth perception depends on a number of factors. Stereopsis and the slight difference in the two retinal images is of importance. Monocular clues of depth are many and are also important. The two most common defects in older people that affect driving are opacities in the transparent optical media and myosis. Driving conditions tend to produce visual fatigue. Vibration at 5 cycles/second causes visual fatigue and reduces perception time.

Since the new automobiles are low, the visibility over the crest of a hill is impaired. To see over the crest, a periscope might be of help.

Fascination and hypnosis are causes of accidents, particularly in modern dual lane highways. Green-tinted windshields decrease vision and should be condemned.

During night driving, glare is an important factor causing accidents. It may be possible to reduce this by increasing the angular size of automobile headlights, by increasing the separation between automobiles, as by the use of dual highways, by highway illumination, and possibly by the use of colored headlights.

The visual reaction time is slow. At high speeds, considerable distance can be covered during the reaction time. Fatigue, alcohol, and distraction will slow the reaction time. 19 references.—*Clement McCulloch, M.D.*

39. *Ocular Manifestations of Traffic Accidents.* M. R. MARSHALL AND S. T. ADAMS. Canad. Services M. J. *12*:245–252, March, 1956.

This summarizes the work of the conference on the medical aspects of traffic accidents and visual problems and gives a number of recommendations that arise from this conference. These recommendations include initial and regular ocular

examination, introduction of systems to obtain significant statistics, and uniform visual standards for all the provinces of Canada, based on the standards given in Dr. Nicholls' paper. The use of periscopes, the construction of dual highways, and indoctrination of drivers in the dangers of fatigue, alcohol, tobacco, and toxic agents are suggested.

In the field of investigation and research is noted the lack of data relating poor visibility and poor visual acuity to traffic accidents. More knowledge is needed concerning the incidence of night accidents with and without green windshields, means of reducing glare from headlights at night, the spectral colors of headlights, the effect of glare itself, and the effect of minus lenses on vision during night driving. 130 references.—*Clement McCulloch, M.D.*

40. *Some Studies of the Applied Psychology Research Unit, Cambridge, with a Bearing on Road Safety Problems.* W. J. SHAW, N. H. MACKWORTH AND R. E. F. LEWIS. Canad. Services M. J. *12*:240–244, March, 1956.

The blinking rate increases when the task is easy and decreases when the task is difficult.

With fatigue, visual alertness and vigilance show a decrement in the form of short discrete lapses. Coincident with the onset of fatigue there is a marked increase in irritability. The response is divergence either toward overaction or toward underaction. Flashing lights that are used as directional indicators should have an off-on ratio of 1:3. The warm-up time of the bulbs should be as short as possible. Frequency should be 180 flashes/minute. 9 references.—*Clement McCulloch, M.D.*

BOOK REVIEW

Clinical Refraction. IRVIN M. BORISH. 575 pages, including 137 illustrations, plus bibliography. The Professional Press, 1954. $9.00.

This is the second edition of this book and it contains approximately one-third more material and illustrations than the first edition, published in 1949. This textbook contains all recent contributions relevant to refraction.

Borish has designed his book primarily for the student and practitioner of optometry. However, much of the contents is instructive to the student and practicing ophthalmologist. The sections on field testing and ocular motility will not be of much interest to the ophthalmologist.

Not only is the field of refraction completely covered, but a detailed account is directed to single vision lenses, bifocals, special lenses, and absorptive lenses. This feature alone justifies the publication of this volume.

The outline organization of the material is a major attribute of this text because all subjects and their component parts are readily found. This arrangement of contents makes the study of refraction easier.

The illustrations are adequate in number and clear in design, which makes the subject more easily and more readily understood.—*Gerald Fonda, M.D.*

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